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ENCEPHALITIS: HISTORICAL REVIEW AND PERSPECTIVE*

HENRY W. WOLTMAN, M.D.,
Rochester, Minn.

Scope of the Inquiry

Today you are taking the measure of an enemy, encephalitis, that remains dangerous and crafty. It is our privilege to place this subject in perspective and, as requested, to include reminiscences of the epidemic of encephalitis lethargica that revealed how complicated and sensitive is the instrument that presides over man's behaviour and destiny.

Inclusively used, the word *encephalitis* has many connotations. Since most forms of the disease will not be referred to again, we shall simply mention, and give an example of, some among the many: mechanical, as in punch-drunk; chemical, as in hydrogen cyanide poisoning; nutritional, as in Wernicke's disease; metabolic, as in porphyria; radiant, as it is encountered after insolation; collagenous, as in lupus erythematous; tænoid, as in cysticercosis; flagellate, as in trypanosomiasis; bacterial, as in undulant fever; plasmodial, as in malaria; spirochætal, as in dementia paralytica; mycotic, as in cryptococcosis; rickettsial, as in Rocky Mountain spotted fever; viral, as in western equine encephalitis, and allergic, as may occur in association with prophylactic vaccination. Now it need hardly be said that effective treatment requires knowledge of the cause.

But proper categorization seems to be lacking if the term *encephalitis* is used without some relation to infection and to the host's response to infection. Therefore, to the physician, the term *encephalitis* comes more easily to mind in the presence of a concatenation of events that bespeaks a diffuse, rather than a focal, cerebral event; a disease that ordinarily has lasted hours or days rather than weeks or months; a disease that is often attended by fever, a change in pulse, headache, nausea, vomiting, clouding of consciousness, some stiffness of the neck, evidence of injury to the brain and the cause of which is not immediately apparent.

The pathologist, hampered by the limited number of ways in which the nervous system can react to injury, and consequently by the similarity of the picture before him to pictures he has seen before, may note injury to nerve cells only; or diffuse or perivascular demyelination; or vascular injury, perhaps with hæmorrhage; or glial and mesodermal response and sometimes, but usually not, the cause.

These two, the practising physician observing a patient who has just become ill, and the pathologist only too often acting as historian, represent extremes, and somewhere between them the battle begins, rages and ends. The great genius of such men as Jenner and Pasteur, working in almost complete darkness, becomes ever more impressive.

A century ago, I. F. C. Hecker[1] wrote, "No epidemic ever prevailed during which the need . . . was not felt . . . to become acquainted with the secret springs of such stupendous engines of destruction." And, indeed, it is easy to think only of the patient and to say almost nothing of the enemy, which is in keeping with an observation made by E. G. D. Murray:[2] ". . . man thinks this is his world, but the microbes don't know that." Rickettsiæ and viruses, like man, are egocentric and, from their standpoint, the invasion of man usually ends in disaster, since they have no means of escape. Viruses seem content to grow and reproduce their kind in birds, smaller mammals, ticks and lice, an arrangement that is often eminently satisfactory to all concerned. But it would be a grave error to infer from this that viruses are easily satisfied. Viruses are exquisitely demanding tenants, exacting from their hosts not only sustenance but also full subsistence, for a vital part of their own struc-

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ture belongs to their hosts. Thus, the very survival of viruses depends on their habitation, which, in turn, determines to a large extent what will happen to man, their accidental host.

The habitation of viruses also forms a basis for their classification. Some viruses are primarily viscerotropic, and only occasionally are they found in the brain. Listed among such, by Olitsky and Casals,[3] are the viruses of herpes simplex, lymphogranuloma venereum, mumps, measles, and, perhaps, infectious mononucleosis. Also among these Donohue, Playfair and Whitaker[4] have cited vaccinia.

Some viruses, although they are not found in the brain, may, in some devious manner, injure it secondarily. For instance, the so-called post-infection, demyelinating varieties of encephalitis are of great neurologic importance because, as A. B. Baker[5] pointed out, there are so many of them. For this reason we shall give as examples only such familiar members of the class as the viruses of chickenpox, smallpox and again, be it noted, measles and mumps. In the category of demyelinating diseases belong also the forms of encephalitis that follow vaccination against (1) smallpox, (2) rabies and (3) whooping cough. Since viruses have not been demonstrated in the brain in these conditions, other explanations of causation, such as toxic or allergic response, have been invoked.

Of special importance to neurologists are the neurotropic viruses that cause encephalitis in man. Best known of these are the viruses that cause poliomyelitis and rabies, which reach the nervous system by a neural route, and the so-called arthropod-borne members: St. Louis encephalitis, Japanese B encephalitis (Japanese A being the von Economo type), Australian X encephalitis, western equine encephalitis, eastern equine encephalitis, and, transmitted to man by direct contact with lower animals, lymphocytic choriomeningitis.

ENCEPHALITIS LETHARGICA, OR VON ECONOMO'S ENCEPHALITIS

Almost every congener of those which compose this type of encephalitis has got out of hand at one time or another. Efforts have been made to identify the nature of epidemics that have occurred since 1695, in which fever, lethargy and ocular palsy or twitching were noted, but the results have been largely conjectural. Therefore, we shall come at once to the epidemic of encephalitis lethargica of which we promised at the beginning we would treat.

Before 1917, only an occasional paper on encephalitis, perhaps caused by lead or by some suppurative process, appeared. Three years after the onset of the epidemic of encephalitis lethargica, communications had passed the 1000 mark and von Economo's[6] name was known to every physician.

In retrospect, this immediate eponymous distinction seemed unusual and after almost 40 years we re-read his paper. It was published in the *Wiener Klinische Wochenschrift*, May 10, 1917, and was entitled "Encephalitis lethargica". Some physicians contend, others deny, that Cruchet, Moutier and Calmettes[7] deserve priority, since their paper was published 13 days before that of von Economo. The French paper appeared in the *Bullétins et Mémoires de la Société Médicale des Hôpitaux de Paris*, April 27, 1917, under the title, "Quarante cas d'encéphalomyélite subaiguë." Thus, it has been said that the disease was born in Paris and christened in Vienna. The chairmen of the sessions at which the papers were presented were distinguished: in Vienna, Wagner von Jauregg; in Paris, Pierre-Marie. Since both reports are of historic interest we shall review them.

Cruchet, Moutier and Calmettes[7] said in essence: Within nine months there were admitted 40 patients with symptoms that suggested pontine, cerebellar and medullary lesions. It was difficult to determine the cause but an attenuated infection was suggested; hence the cases were classified as examples of subacute encephalomyelitis. The general characteristics were as follows: onset with extreme lassitude; absence of violent headache; fever generally absent but at times a feeble elevation of temperature. The inert facies, indifference, semistupor, emaciation, earthy colour and lack of appetite of these patients suggested infection or intoxication. The authors mentioned only the clinical varieties: (1) the mental variety, with torpor, amnesia, disorientation, pupillary changes, tremor, dysarthria, paraphasia and changes in the spinal fluid; (2) the convulsive variety; (3) the choreiform variety; (4) the meningitic variety; (5) the hemiplegic variety; (6) the pontocerebellar variety, with ptosis, conjugate paralysis and titubation; (7) the bulbopontine variety, with involvement of nerves, such as the trigeminal, facial and vagospinal nerves; (8)

the acute ataxic variety, suggestive of toxic-infectious polyneuritis and (9) the anterior poliomyelitic variety. Often the cases were polymorphic. Two patients died; recovery of the others was interminable, with retention of anatomic lesions. Cruchet and his associates were poorly situated to carry out investigations.

Von Economo[6] said in essence: Since Christmas, he and his associates had observed a group of patients whose illness did not allow it to be classified under any of the customary diagnoses. It was a sort of sleeping sickness. The symptoms began acutely, with headache and malaise, but these were followed by a state of somnolence, which often was associated with lively delirium. The patient might be awakened easily and he gave evidence of comprehending the situation; he carried out commands correctly and could walk and stand, but, left to himself, he again fell asleep. This delirious somnolence might end in death or it might fluctuate from drowsiness to deepest coma for weeks or months, and then improvement might occur, to be followed by a long period of psychic asthenia. In mild cases drowsiness might be followed by palsy. Symptoms of meningeal irritation never were striking. There might or might not be fever and, if present, it bore no relationship to the other symptoms. Generally some involvement of the ocular muscles was added; indeed, this might be the first symptom. The increased incidence of the condition suggested that a small epidemic was in course.

Abstracted reports of seven cases were given. Laboratory data were included in all and necropsy findings in two. In six cases the spinal fluid was clear, generally under increased pressure and sterile; the concentration of protein was slightly increased and cell counts generally ranged from 5 to 19 per cubic millimetre; one however was 43.

Necropsy disclosed (1) increased fluid in the subarachnoid space; (2) hyperæmia of meninges, cortex and both anterior and posterior horns of the spinal cord at the level of the thorax; (3) definite small round-cell perivascular infiltration, more in the grey matter than in the white and in the regions of the third ventricle, the ocular nuclei, the aqueduct and the floor of the fourth ventricle; (4) foci of neuronophagia in the cortex. The meninges were not heavily infiltrated.

Von Economo[6] also referred to six patients, seen in the out-patient department, who had not been somnolent or delirious but who had been observed to make choreiform movements and to have fixed pupils.

Von Economo concluded his article with the following sentence: "We think therefore that this encephalitis, of mildly epidemic incidence, with the characteristic symptom of somnolence and the peculiar anatomicohistologic findings, is a specific disease *sui generis*, caused by a specific living virus which, as indicated by the strikingly minimal general symptoms and the intensity of the cerebral symptoms, has a specific affinity for the central nervous system, similar to, but not identical with, the virus of poliomyelitis (Heine-Medin)."

Neither Cruchet and associates nor von Economo realized that they were witnessing the beginning of an epidemic that almost at once took off for Australia, England, South America, Africa, North America and Asia. Almost simultaneously, a great pandemic of influenza got under way. In different places and at different times, separately or concurrently, both epidemics swept the earth.

This epidemic of encephalitis was unusual not only because it became pandemic but because it produced a previously unrecorded spectacle of motor and mental chaos; because its manifestations changed almost completely from time to time, often suggesting an entirely new disease; because the illness was followed, or often the fact of its former presence first was revealed, by strange sequelæ and because, as the years passed, the case incidence became smaller while the number of patients became larger. One may search in vain for some thread of continuity.

Mayo Clinic Experience.—What we shall say now is based mainly on a follow-up study of 752 patients who were examined at the Mayo Clinic, the results of which study were reported by Ziegler[8] in 1928, and on information gleaned from the records of 313 patients whose cases he did not include.

The first patients with encephalitis lethargica appeared in the winter of 1918-1919. The incidence of acute cases of the disease was highest in 1920 (180 cases) and again in 1923 (111 cases), after which the epidemic subsided gradually, to disappear about 1927. January and February were the worst months. Most patients were less than 40 years of age but no age group was exempt. Among Ziegler's cases, the onset of the illness was acute in 85% and was unappar-

ent in 15%. The acute attack lasted from two days to four months and 32% of patients died (see Ziegler's table 3). Sleep was disturbed in 84% of cases and diplopia was present at one time or another in 47%. Sequelæ immediately followed the acute illness in 50% of cases; in others, onset of sequelæ was delayed, sometimes for years, and as already noted, might be the first indication of encephalitis. Although, in the acute phase of the illness, most patients slept and many had diplopia, others exemplified a different syndrome.

For example, a boy, about 15 years of age, who was seen in a village near Rochester, had been ill about five days. His doctor said, "Fever has been very mild." His mother added, "But he is so different. He stands there most of the time with his mouth open and doesn't say a word." He was, indeed, a pillar of parkinsonism.

As the seasons passed, and new sequelæ appeared, we of the clinic staff said on more than one occasion, "hysteria". A boy of seven years, for instance, said he could not get his breath; yet at times he breathed hard and noisily. He could run a block and he never had trouble when he rode horseback. But then too many like him appeared, and some had parkinsonism. An exuberant infant kept her parents awake by playing and jumping about in her crib all night. There were also too many of these. Then many patients could not sleep. "Muscular impatience" was common. Pacing the corridors of a hospital, one might see a woman who, with each step of the left foot, would slide the toe of the right foot from the left ankle to knee before planting the lifted foot on the floor. In a waiting room, the source of a long, frightening howl might be the cavernously opened mouth of some woman who was seated among other patients.

Most common were motor disturbances: tremor; rigidity; dystonic movements, repetitious or peripatetic; motor arrest, local or general, fleeting or lasting hours; contortions of face and tongue, opening of the mouth, clenching of jaws, grinding of teeth; blinking; uncontrollable laughing; cascading or repetitious speech; oculogyric crises; attacks of deep breathing, salaaming and breath-holding. Convulsions almost never were seen.

Also there were autonomic and endocrine disturbances: intolerance to heat; sweating; seborrhœa, especially of the face, to which the term "Salbengesicht" was applied; polydipsia; disturbance in sugar metabolism; real or simulated hyperthyroidism; eroticism; loss in weight, gain in weight; incontinence or retention.

Not uncommon were psychiatric disorders. Especially among the young were idiocy and behaviour disorders that led to Hall's[9] designating some of them as members of an apache group and others of them as members of a group of difficult children. Affective, schizoid and paranoid disorders, irritability and rages, and asthenia and social ineffectiveness also were observed.

Some of the phenomena were almost pathognomonic of the disease. In the early twenties of this century, the abdomen was inspected carefully. Swift, lateral displacements of the umbilicus confirmed the diagnosis of suspected encephalitis. The occasional association of the abdominal twitching with movement elsewhere suggested that the twitch did not originate at a spinal segmental level.

The most common sequel among Ziegler's[8] 752 patients was parkinsonism. It occurred in 78% of cases and usually was marked by greasiness of the face; salivation, called *wet tongue* by Wilson;[10] a high incidence in the young, and other encephalitic stigmata. Ziegler followed up his patients an average of 5.5 years after the acute attack. Review of the records of the 313 patients not included in Ziegler's series disclosed that of 99 of them who had parkinsonism, the acute attack of encephalitis could be dated. Of these 99 cases, in 42 parkinsonism appeared within the first five years after the acute attack; in 29, within the second five years, and in 21, within the third five years. In the remaining seven cases, parkinsonism appeared from 16 to 31 years after the acute attack. The report in 1928, in which it was said that 1.3% were well, may have been too optimistic.

Oculogyric crises, mentioned earlier, occurred in 4% of Ziegler's cases. Sometimes, on the intrusion of a compulsive thought, such as the need of adding a set of digits, the eyes would slowly turn upward and remain in that position for minutes or hours. Occasionally the eyes turned laterally or downward. Common bedfellows other than parkinsonism were dystonia, yawning, champing, outbursts of temper and blinking.

Blepharospasm, or to follow Harry L. Parker's reintroduction of the term, *paraspasme facial*,

was about a fourth as common as were oculogyric crises, and half of the patients who had paraspasm also had parkinsonism. Patients with paraspasm observed that their eyes might open suddenly if they became frightened, and many discovered tricks that relieved them of the spasms. For instance, one patient, a physician, could drive to see his patients if he sang or yodelled all the way; later he became parkinsonian. A dentist could carry on his work by whistling; he too acquired parkinsonism. Several patients kept their eyes open by playing with a toothpick held between their lips and one woman learned that chewing spruce gum was the best remedy.

Not uncommon was the respiratory syndrome; the incidence was 9% in Ziegler's[8] series. In the spring of 1920, a girl, 5 years of age, had what was called *intestinal flu*. When she reached the age of 10 years, she became very sleepy and had trouble breathing. Six to ten deep respirations, taken while she leaned far backward, were followed by holding the breath and bending forward until she became blue and at times lost consciousness. Meanwhile saliva streamed from her mouth. At the age of 12 years, parkinsonism appeared. By the time she was 19, she spent most of her time in bed on her hands and knees, still having attacks. When she became excited or angry, her breathing was normal. She died in 1942, 22 years after the onset of her illness.

Disordered behaviour was a sinister sequel, particularly if the patient was a child. Kennedy[11] found that among children who had sequelæ of encephalitis, they took the form of behaviour disorder in 45%. He gave as an example the history of a boy, aged 10 years, who had to be taken out of school because he asked so many questions, took books from other children and slept often. He stole a diamond and disposed of it so that he could ride in an automobile. Later, he entered stores and gave the objects he had taken to people—to be good to them. He ran away and slept in churches and on porches. He begged food, saying that his parents had died. He prayed at inappropriate times, threw kisses, set fires, and one could not believe a word he said.

In 1924, Kennedy[11] traced 51 children who had one sequel or more. In 23 there had developed changes in personality and behaviour; in 21 who were between the ages of seven and 14 years, parkinsonism; in 20, respiratory disturbances; in 19, disturbance of sleep and nocturnal hyperkinesis.

Sixteen years later (1940), Heersema[12] was able to study 40 of Kennedy's 51 patients from the standpoint of social adjustment. Whereas, in 1924, the outlook had appeared hopeful for 43% of the 51, by 1940 the condition of only 18% of 40 had improved.

Rather early in the epidemic it was conceded that once parkinsonism developed it was probably there to stay, but for some time a more hopeful view prevailed regarding other sequelæ. This view proved to be not fully justified.

At the Rochester (Minnesota) State Hospital is a woman, 64 years of age, with an extensive repertory of sequelæ. She had lethargic encephalitis in 1924. When she left the hospital after an initial stay of three months, her right arm was trembling, and it still trembles. One year after onset of the encephalitis, spells of blinking began; she still blinks. Now these spells are accompanied by her hearing bursts of some trisyllabic phrase that she must add. Ordinarily a gentle creature, she may, when the voices and blinking are too persistent, fly into a rage, curse or kick someone. She has oculogyric crises. She also has attacks of motor arrest without loss of consciousness or, as patients often call them, *stopping spells*. She may be seen bent over a water fountain as if frozen there; or she may stand in the washroom like a statue with her jeans raised to mid-thigh; or her hand, holding a sandwich, may be arrested halfway between the plate and her mouth. Usually it is only her face that is affected in such a stopping spell and then she cannot speak, an instance of akinetic mutism. The stopping spells, which may last from one hour to two days, often end with a drenching sweat.

The number of patients who had epidemic encephalitis and who later entered state hospitals cannot be estimated at this time. Dr. M. C. Petersen, superintendent of the Rochester State Hospital, and Dr. J. A. Lazarte, assistant superintendent, both of whom retain great interest in neurology, promptly recalled the names of 23 psychotic patients who had had encephalitis. Of these, 14 had had encephalitis lethargica. Of the 14, 10 have parkinsonism, two have akinetic attacks, and two, who had had encephalitis at the ages of one and four years respectively, are mentally deficient and psychotic. The high

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incidence of assaultive behaviour, in five of the 14 patients, we were told is far more than average. Two of the 14 had strabismus and the pupils of three of the 14 reacted to light but not to convergence; this is a fairly common finding in cases of encephalitis lethargica.

The cause of the encephalitis that von Economo described was not found nor will it be found. New viruses are discovered every few weeks, and if the virus of the disease that von Economo observed is among them its name does not suggest the sought association. Nor is it known what caused the sequelæ. Perhaps, as Greenfield and Matthews[13] suggested, they reflect some continued action of the virus in a modified form.

THE ARTHROPOD-BORNE VARIETIES OF ENCEPHALITIS

The flood of some 5000 titles on encephalitis lethargica ended shortly before 1933 when an epidemic of encephalitis occurred in St. Louis. Koch's postulates were fulfilled, and before the year was out the cause was known. Everything achieved about this time cannot be mentioned here. However, in 1936, the virus of "Japanese encephalitis" had been found. In 1937, the virus of Russian Far East encephalitis, tick-borne, was discovered. In 1938, the viruses of western equine encephalitis and of eastern equine encephalitis were recovered from man. Nor are these all, but their mention suffices to show the pace that has been set and the advances that have been made in the field.

It appears that in North America the eastern viral diseases are moving westward, the western ones eastward and that the continental plain will soon harbour all. And epidemics may be expected. Optimal conditions for large epidemics are few and usually not apparent, since they involve such factors as conditions of weather, migrations of birds, the presence of insects and of epizootics, states of immunity, mutants and coincidence of epidemics.

That sequelæ also are characteristic of the arthropod-borne varieties of encephalitis already has been shown by surveys, such as those made by Mulder[14] for the Colorado epidemic, by Finley and co-authors[15] for the California Central Valley epidemics and by Fulton and Burton[16] in the Battleford and Weyburn provincial hospitals.

What has been learned of epidemics since Hecker[1] urged physicians "to become acquainted with the secret springs of such stupendous engines of destruction" is impressive. What is even more impressive is that such knowledge can be, and is being, utilized effectively. Perhaps experience makes inevitable the neurologist's greater concern with sequelæ than with the disease itself. In encephalitis the most effective measure in dealing with sequelæ is to prevent the disease. Fortunately the prospect of doing just this is bright.

Much of the credit for knowledge of viral forms of encephalitis should be assigned to the pioneering efforts of veterinarians. With the cooperative endeavours of physicians, virologists, immunologists, epidemiologists and scientists in other fields, to adapt Aristotle's figure to the present purpose, the knot is becoming known and is being untied. Said Sir Charles Bell,[17] whose memory is a notable example for the clinician, "Gentlemen, wise men pursue some determined object. . . . None will hesitate to say that it is our duty to observe accurately when an accident may be converted into an experiment."

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RÉSUMÉ

"L'homme croit que la terre lui appartient, mais les microbes n'en savent rein", disait E. G. D. Murray. En effet les virus sont des hôtes des plus exigeants lorsqu'ils envahissent l'organisme humain. Même ceux qui n'appartiennent pas au groupe neuro-tropique, à savoir, ceux que l'on trouve habituellement dans les viscères, peuvent malgré tout causer un retentissement cérébral important. Telles sont les encéphalites démyélinisantes post-infectieuses de la variole, de la varicelle, de la rougeole et des oreillons.

Le 27 avril 1917, Cruchet, Moutier et Calmettes publiaient leurs observations sur "40 cas d'encéphalomyélite subaiguë," suivies quelques jours plus tard par un article venant du camp opposé signé de Von Economo sur une maladie semblable qu'il appelait *encéphalite léthargique*. On y décrivait de part et d'autre le tableau clinique d'une affection qui devait devenir avec l'influenza le point de départ d'une pandémie qui atteignit presque tous les points du globe. Le tableau clinique du début se modifia à mesure que la maladie se propageait. Les sequelles que l'on avait observées dans 50% des cas immédiatement après l'atteinte initiale se révélèrent de plus en plus nombreuses, et quelques unes apparurent seulement 20 ou 30 ans après la phase aiguë de l'attaque.

L'auteur fait part ici des faits cliniques que put observer le personnel du département de neurologie de la clinique Mayo chez plus de 1,000 cas d'encéphalite léthargique suivis pendant plusieurs années. L'épidémie apparut aux Etats-Unis dans l'hiver de 1918-19, sévit pendant plusieurs années et disparut graduellement vers 1927. La majorité était composée de sujets de moins de 40 ans bien que tous les âges en fussent atteints. Si les principaux symptômes étaient la somnolence et la diplopie, on n'en nota pas moins une foule d'autres tels que des impatiences musculaires, de l'insomnie, des tremblements, de la rigidité, des contorsions, de la persévération, des crises oculogyres, des troubles neurovégétatifs et endocriniens ainsi que des altérations du comportement et des perturbations psychiques. Le syndrome parkinsonien suivit l'infection dans 78% des cas.

Il est peu probable que le virus que soupçonnait Von Economo ne soit jamais identifié. Peut-être l'a-t-on déjà isolé depuis sans que rien ne puisse indiquer maintenant qu'il ait été jadis responsable de ravages si redoutables. L'encéphalite léthargique céda la vedette en 1933 à l'encéphalite de Saint-Louis qui fut elle-même suivie de plusieurs autres depuis.

NASAL CARRIAGE OF STAPHYLOCOCCUS PYOGENES BY STUDENT NURSES*

I. B. R. DUNCAN, M.B., Ch.B.,
ANNE M. COLLINS, M.Sc.,
ELISABETH M. NEELIN, B.H.Sc., and
T. E. ROY, M.D., *Toronto*

MUCH INFORMATION has been accumulated in recent years about the carriage of *Staphylococcus pyogenes* in the human nose. Williams[1] in 1946 showed that skin carriage of staphylococci was secondary to nasal carriage, and that nasal carriers could be separated into those who harboured staphylococci constantly and those in whom carriage occurred only sporadically. Gould and McKillop[2] examined a large group of university students at weekly intervals for many months and were able to classify carriers further into three types: persistent, intermittent, and occasional. These workers also noted that some students never at any time carried staphylococci in the nose.

Many studies have been made of carriage of staphylococci by hospital nurses. These have shown that the carrier rate among them is higher than in the population outside hospital, and that nurses frequently harbour antibiotic resistant staphylococci, particularly strains causing cross-infection among patients. A number of investigators have made serial examinations of new entrants to nursing during their early hospital training to determine the increase in carriage during training, and the stage of training at which they acquire hospital strains of staphylococci. In three of these surveys[3-5] a marked increase was noted in the carrier rate within four or five weeks after the nurses finished their preliminary training and began ward duties. Hutchison and his colleagues[6], however, found no such increase in the number of carriers in the course of a long and careful survey of new nurses. All four groups of workers found that the nurses acquired antibiotic resistant staphylococci more frequently when they went on ward duty.

The object of the present investigation was to determine whether the increase in nasal carriage which has been described in nurses going on ward duty represents an increase in true long-term carriers, and to determine which hospital strains tend most readily to colonize the nose.

POPULATION STUDIED

In this hospital, new classes of student nurses begin training every six months. They spend four to five weeks in full-time classroom training and then work on the wards for only a few hours weekly until the 18th week, when they begin full-time ward duty. Three such classes took part in the study. Only three of the nurses in the first two classes and four in the third class had previous contact with a hospital, either

*From the Research Institute of the Hospital for Sick Children and the Department of Bacteriology, University of Toronto. Assisted with funds allocated by the Province of Ontario under the National Health Grants program of the Department of National Health and Welfare, Ottawa.

as patients or nursing assistants. The details for each class studied are as follows:

Class 1—42 nurses. Weekly nasal swabs were taken for 18 months except when the nurse was affiliated to another hospital or was not available for other reasons. Fewer examinations were possible towards the end of the survey. The number of weekly swabs obtained from individual nurses varied from 30 to 48, with an average of 39, for the first 52 weeks; and from 37 to 63, with an average of 50, for the whole 78 weeks of the survey.

Class 2—9 nurses. Weekly nasal swabs were taken over a period of a year. The number of swabs obtained from individual nurses varied from 25 to 43 and the average was 31.

Class 3—53 nurses. Only a limited survey was undertaken. Nine swabs were taken from each nurse, two in successive weeks at the beginning of training, three in successive weeks in the fourth month of training, and four in successive weeks in the eighth month of training.

Laboratory Staff—For comparative purposes, a group of 15 bacteriology laboratory staff was examined. Twelve were followed up for 20 months, and three for nine months. Nasal swabs were taken weekly for the first 20 weeks and, because of the consistent findings in this group, at monthly intervals thereafter.

METHODS

Specimens were taken by rotating a moist cotton swab three or four times inside both nostrils. The swab was spread on a sheep blood agar plate, and was then placed in a tube of Maitland and Martyn's enrichment broth for staphylococci.[7] The broth was subcultured to blood agar if no staphylococci were isolated from the original plate. On the basis of cultural characteristics, one or more colonies were picked for coagulase testing. If coagulase positive (*Staphylococcus pyogenes*), they were tested for sensitivity to penicillin, tetracycline, chloramphenicol and erythromycin by a disc-plate method using the low and high strengths of Difco Disks for each antibiotic. All *Staph. pyogenes* isolated in the first year of the survey were typed with bacteriophage. Twenty phages were used, all of the international basic set,[8] except 71 and 80, and, in addition, phage 81 which lyses many staphylococci isolated in Canada.[9] Strains of phage and the strains of staphylococci on which to propagate them were generously supplied by Dr. E. T. Bynoe of the Laboratory of Hygiene, Ottawa. Typing was done first with phage at routine test dilution (R.T.D.), and strains which failed to type were later retested with phage at 100 x R.T.D. Occasionally, even if all colonies on a plate appeared similar, up to six colonies were picked for phage typing to determine whether more than one strain was present. Antibiotic sensitivity patterns were used in conjunction with phage types in determining whether strains were the same.

TYPES OF CARRIER

Fig. 1 illustrates the various patterns of carriage found in individual nurses and gives the number in classes 1 and 2 showing each pattern.

Constant carrier—Staph. pyogenes was cultured from the nose, usually in large numbers at almost every examination. In four nurses (8%), the same strain was isolated each time, and another four (8%) were constant carriers whose strains varied from time to time. In these, either the replacing strain overlapped the original one and eventually replaced it entirely, or a second strain was harboured for a time along with the original strain, and then disappeared. Rarely 3 different strains were present simultaneously. All these features of constant carriage are shown in the chart. Some nurses were classed as constant carriers even though they had negative swabs for varying short periods, but they seemed to fall into this classification rather than into the intermittent group. Constant carriers accounted for 16% of the nurses.

Intermittent carrier—Here, periods of consistent carriage alternated with similar periods of non-carriage. Consistent carriage is defined as the carriage of a strain of *Staph. pyogenes* for several weeks. This is considered true colonization. There were nine intermittent carriers (18%) whose colonizing strains remained the same; 13 (25%) carried different strains at each period of colonization. There were great differences in this group in the lengths of these periods of colonization, varying from 14 months' carriage followed by four months' non-carriage to colonization for only the last month of the survey. The differentiation of intermittent and constant carriers in borderline cases was somewhat arbitrary, but intermittent carriers could be distinguished from occasional carriers much more readily since only the intermittent carriers showed true colonization. A colonizing strain was recovered from 42% of all swabs taken from intermittent carriers. In addition, intermittent carriers occasionally, during phases of non-carriage, briefly harboured strains which failed to colonize the nose. In the whole group of nurses, 43% were intermittent carriers.

Occasional carrier—Small numbers of *Staph. pyogenes* were isolated on rare occasions in

this group, which consisted of 18 nurses (35%). In some a different strain was recovered on each of four or five occasions. In others, one strain was recovered on one occasion only. In a few, the same strain was isolated from two successive swabs, but these nurses seemed to fit better into the group of occasional rather than intermittent carriers. Each occasional carrier had an average of three positive swabs during the whole survey.

Non-carrier—This small group of three nurses (6%) consists of those from whom *Staph. pyogenes* was never isolated. It seems probable that these nurses do not differ significantly from occasional carriers. In both, a staphyococcus from the air must contaminate the nose periodically. Should this be recovered from a culture taken shortly afterwards, the individual would be classified as an occasional carrier. Non-carriers and occasional carriers together made up 41% of the group. In a few non-carriers, even the usual nasal flora of *Staph. albus* and diphtheroid bacilli was unusually scanty.

The laboratory staff showed the same patterns of carriage as the nurses, but fitted more readily into the different patterns. Of the 15 laboratory workers, six (40%) were constant carriers, four (27%) were intermittent carriers, two (13%) were occasional carriers, and three (20%) were non-carriers. Each constant and intermittent carrier had a single colonizing strain throughout.

Patterns of Nasal Carriage of Staphylococci

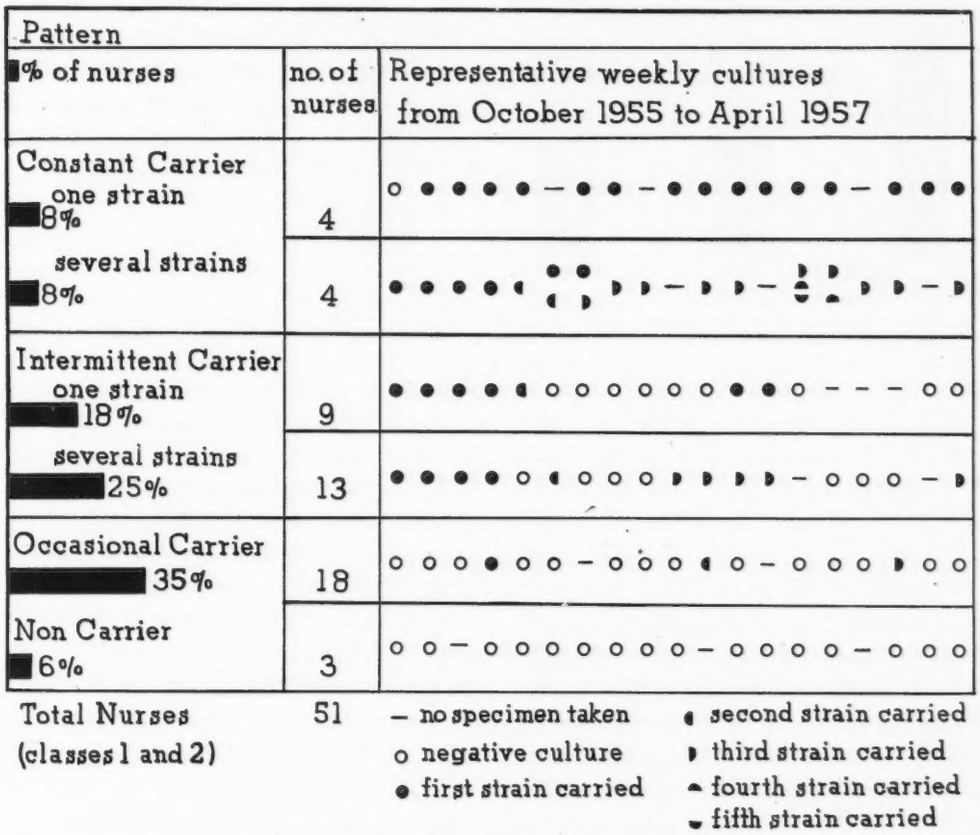

Fig. 1.—Patterns of nasal carriage of staphylococci.

INFLUENCE OF HOSPITAL ENVIRONMENT ON CARRIAGE

Carriage rate – It is evident from the different patterns of carriage encountered that the calculation of carriage rates from the number of positive swabs on any one day is inadequate. Such figures will include as carriers those occasional carriers who happened to harbour a few staphylococci at the time of swabbing. Another variation is introduced by occasional negative swabs from consistent carriers. These inaccuracies are apparent in the following carrier rates calculated for class 1 on a number of representative weeks: 1st week – 33%; 4th – 24%; 7th – 43%; 8th – 34%; 10th – 48%; 12th – 41%;

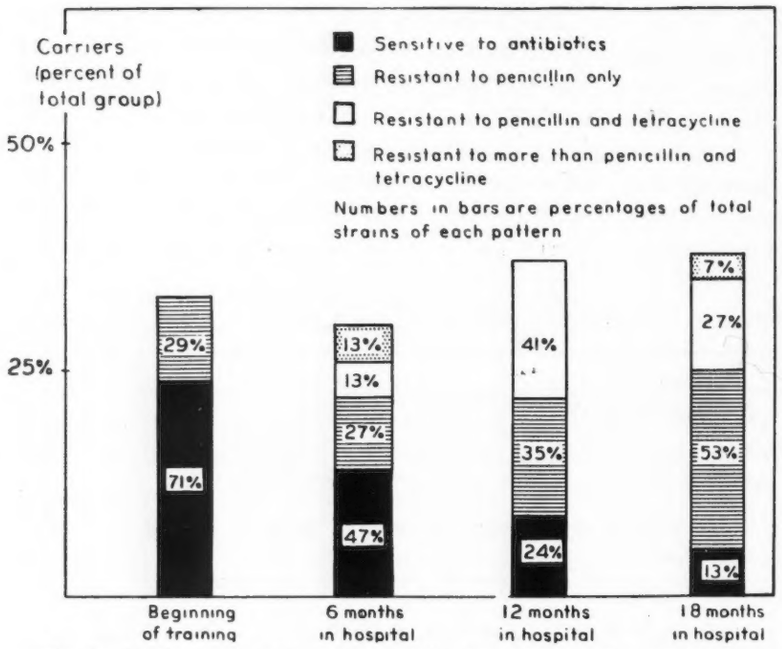

Fig. 2.—Incidence of carriers and antibiotic sensitivity of carried strains. Results from classes 1 and 2 (51 nurses).

15th – 38%; 21st – 37%; 25th – 24%; 32nd – 35%. It is clear from these figures that no valid comparisons can be made between carrier rates on different occasions if they are based on limited surveys.

A much better estimate of carriage rate would be one based on three or four consecutive weekly examinations from which might be calculated the proportion of individuals carrying staphylococci consistently. Fig. 2 shows carriage rates calculated in this way at the beginning, at 6 months, and at 12 months for classes 1 and 2, and at 18 months for class 1. Over the whole period, there was little change in the carriage rates, which remained between 30 and 38%. The rates for 53 nurses of class 3, calculated in the same way, were 36% at the start of training, 40% in the fourth month, and 28% in the eighth month.

Types of strains carried – While the carrier rates in nurses remained fairly constant throughout, there was a marked change in the type of strains carried, as shown by patterns of antibiotic sensitivity and phage types. The changes in antibiotic sensitivities are shown in Fig 2.

At the beginning of the nurses' training, 71% of the carried strains were sensitive to all antibiotics, but by 18 months only 13% were sensitive. Strains resistant only to penicillin increased from 29% at the beginning to 35% at 12 months. At 18 months, there had been a further increase to 53%, but the series was smaller. Penicillin-tetracycline resistant strains were not found at the beginning but by 12 months were 41%, and at 18 months were 27%. A few strains with other patterns of resistance were found at six months and 18 months.

With one exception, the penicillin-tetracycline resistant strains which appear in Fig. 2 were found to be of phage type 81. Most strains were lysed by this phage at R.T.D., but a few reacted only at 100 x R.T.D. The single strain failing to react was only tested at R.T.D. A few strains were also lysed by phages 52 or 52A. Strains sensitive to antibiotics were of various phage types, with a number failing to type. Strains resistant to penicillin only were mostly of group III, and those resistant to more antibiotics than penicillin and tetracycline were all of group III.

The nurses of class 3 also acquired, as their colonizing strains, more staphylococci resistant to penicillin and tetracycline than staphylococci

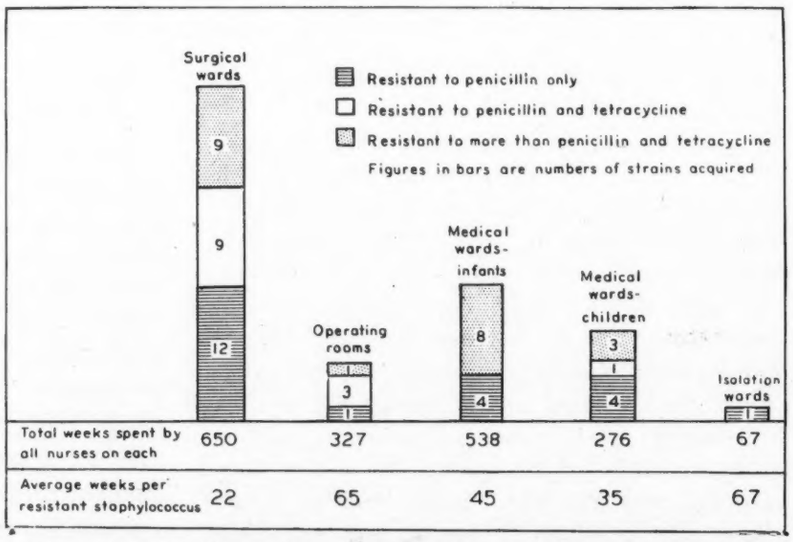

Fig. 3.—Wards where nurses acquired resistant staphylococci. Results from classes 1 and 2 (51 nurses).

of other patterns of resistance. At the eighth month of training, 26% of the carriers were consistently carrying penicillin-tetracycline resistant strains.

Differences within the hospital – Fig. 3 shows the relationship between the acquisition by nurses of antibiotic resistant staphylococci and the different parts of the hospital in which they worked. This analysis includes all resistant strains isolated, both colonizing and transiently harboured ones. On the surgical wards, the nurses of classes 1 and 2 picked up 30 resistant strains; 12 were resistant to penicillin only, nine to penicillin and tetracycline, and nine to more antibiotics. A total of 650 weeks was spent by the members of the two classes nursing on these wards. Thus, on an average, a resistant staphylococcus was acquired by a nurse every 22 weeks. Nurses in the operating rooms acquired resistant strains less frequently, on an average once every 65 weeks. In the infant medical wards, 12 strains were acquired, four resistant to penicillin alone, and eight to more antibiotics than penicillin and tetracycline. There, the nurses spent 538 weeks, and the average number of weeks to acquire a resistant staphylococcus was 45. In medical wards for older children, the average was 35 weeks. Only one strain was picked up during the 67 weeks spent by the nurses in the isolation wards. These figures show that there is a considerably greater chance of contamination of a nurse's nose by resistant staphylococci when she is working in the surgical wards than in the medical wards. It also appears, though the numbers involved are small, that the careful nursing procedures of the isolation wards lessen the chance of nasal contamination by resistant staphylococci in spite of the segregation in these wards of a large number of cases of staphylococcal sepsis.

The bacteriology laboratory environment had no influence in changing carried strains. All the constant and intermittent carriers kept the same colonizing strain throughout the survey, and these were either fully sensitive or resistant to penicillin only. The two occasional carriers had two positive cultures each during the whole survey, and these strains were fully sensitive or resistant only to penicillin.

NASAL COLONIZATION BY ANTIBIOTIC RESISTANT TYPE 81 STRAINS

Staph. pyogenes of phage type 81 and resistant to penicillin and tetracycline was carried for lengthy periods by a number of nurses, but other strains of staphylococci, although picked up frequently, less often remained as the colonizing strain. Long periods of colonization by penicillin–tetracycline resistant type 81 strains were observed on 10 occasions, but on only five was this strain found at a single isolated weekly examination. Thus, two out of every three times that the strain was found in a nurse's nose, it remained for many weeks as the colonizing strain. At the end of the survey, six were still present after being carried for periods of four, five, 13, 24, 44, and 48 weeks; four others were carried for 14, 17, 33, and 49 weeks.

Type 81 strains of other patterns of sensitivity were few; two were isolated only once, two were found as colonizing strains and one was carried by a nurse when she began training.

With group III strains resistant to more antibiotics than penicillin, there were six episodes of colonization and 18 occasions when the staphylococcus was found only once. Thus, these strains succeeded in colonizing the nose on only one of every four occasions they were encountered. Moreover, they remained as the colonizing staphylococcus for relatively short periods—two, three, six, seven and 13 weeks; one remained for 16 weeks and was still present at the end of the survey.

With antibiotic sensitive strains, there were 14 periods of colonization and 28 single isolations. With strains resistant to penicillin only, there were 16 periods of colonization and 21 occasions when the strain was isolated once. These strains include all phage types and some strains which were not typed.

In all, there were 36 periods of colonization during the survey by strains other than the penicillin-tetracycline resistant type 81, and 70 occasions when these miscellaneous strains were found on only one examination. This finding of one out of three contrasts with that found with the penicillin-tetracycline resistant phage type 81 and suggests that this strain has a greater tendency to colonize the nose than other staphylococci.

PHAGE TYPES

The phage types of 113 *Staph. pyogenes* of each pattern of antibiotic sensitivity isolated from nasal swabs from nurses during the first year of the survey are given in Table I. A strain isolated repeatedly from the same carrier

TABLE I.

Phage pattern	Sensitive to all		Penicillin resistant		Penicillin-tetracycline resistant		Other patterns	
	Nurse	Patient	Nurse	Patient	Nurse	Patient	Nurse	Patient
I. (R.T.D.)	9	—	2	—	—	—	—	—
I. (100 x R.T.D.)	1	—	—	—	—	—	—	—
II. (R.T.D.)	4	5	7	6	—	—	—	—
II. (100 x R.T.D.)	2	—	—	—	—	—	—	—
III. (R.T.D.)	4	1	12	2	3	7	21	11
III. (100 x R.T.D.)	5	—	4	—	—	—	—	—
81. (R.T.D.)	1	4	—	11	13	60	2	6
81. (100 x R.T.D.)	1	—	1	—	2	—	—	—
Mixed Group	1	—	1	4	—	1	—	—
N. T.* (only done R.T.D.)	2	18	1	11	1	7	—	1
N. T. (100 x R.T.D.)	12	—	1	—	—	—	—	—

*Not typable.

is considered a single strain in this analysis. Strains isolated only once are included. A separate series of 155 strains isolated from infected patients in the hospital was examined, and the phage types of strains of each sensitivity pattern are also shown in Table I.

The strains in both series were generally similar. Antibiotic sensitive strains and those resistant to penicillin only were distributed among the various phage groups. Most penicillin-tetracycline resistant strains from both sources were phage type 81, and this particular strain was the most frequent among staphylococci from patients. Strains resistant to more antibiotics than penicillin and tetracycline were almost all of group III; the remainder were type 81.

Type 81 strains isolated from patients and nurses were of practically all patterns of resistance from fully sensitive to resistant to penieillin, streptomycin, tetracycline and erythromycin, but few were fully sensitive. A number of group III strains showed lysis with phage 81 as well as with most of the group III phages. Type 81 seemed to share with group III staphylococci a marked tendency to be resistant to antibiotics.

IN VITRO INVESTIGATIONS

Strain replacement.—As described above, strain replacement was noted frequently in many carriers. Experiments were carried out in an attempt to explain this phenomenon. It was not found that the replacing strains could overgrow the replaced strains in broth. Such tests could be readily done when the strains differed in sensitivity, by carrying out viable plate counts on antibiotic-containing media. Attempts to detect the formation of antibiotic or other inhibitory substances by the replacing strain were unsuccessful. One replacing strain was shown to be carrying a phage capable of lysing the original strain. This finding could not be demonstrated with any of the other pairs of replacing and original strains.

Differences between carriers and non-carriers.—No correlation was found between carriage and abnormalities or infections of the nose or nasal sinuses. No consistent differences were found in the type of aerobic flora, other than *Staph. pyogenes,* of carriers and non-carriers. Tests so far have failed to show that the commensals in the noses of non-carriers produce substances capable of inhibiting *Staph. pyogenes.* Preliminary investigations have not revealed any marked differences in the lysozyme content of the nasal mucus of carriers and non-carriers. Strains of staphylococci from carriers have been tested for sensitivity to both nasal lysozyme and crystalline egg-white lysozyme and no bacteriostatic or bactericidal effect has been demonstrated.

DISCUSSION

The patterns of carriage described by Gould and McKillop[2] seem broadly applicable to hospital staff, although they were originally found in a predominantly non-hospital population. It is noteworthy, however, that the members of the bacteriology laboratory staff fitted the carriage patterns more closely than the nurses.

The nurses, being exposed to numerous staphylococci on the wards, showed a greater variation in carriage pattern within the four broad groups. Perhaps an equally satisfactory subdivision would be the grouping together of constant and intermittent as true carriers, and of occasional carriers and non-carriers as those peculiarly resistant to nasal colonization, and thus in effect non-carriers. Hutchison and his colleagues[6] also found that a proportion of nurses, despite the presence of many staphylococci in the ward environment, failed to become carriers. There seems little doubt that these individuals possess some host factor which prevents colonization by staphylococci. Our own experiments are not sufficiently far advanced as yet to prove or disprove the theory advanced by some workers that there may be differences in the lysozyme content of the nasal secretions of carriers and non-carriers. The very scanty total nasal flora in some of the non-carriers in our group might favour a non-specific mechanism but specific immunity may play a part. The absence to date of a satisfactory test for antibacterial antibodies against the staphylococcus as distinct from antitoxins seriously hampers the investigation of specific immunity, which might be effective locally.

The fairly constant carriage rate during the first 18 months of training in the nurses in this study is at variance with the findings of many workers. This is probably because most investigators have included occasional carriers by making use of the single swab survey. It is misleading to classify as a carrier a nurse of the occasional carrier group who has only a few contaminating staphylococci in her nose on isolated occasions. It has been shown that nurses picked up far fewer staphylococci in some wards of the hospital than in others, and that fewest were acquired in wards where nursing techniques and infectious isolation procedures were most efficient. Similar differences probably exist from one hospital to another, so that nurses in different hospitals would vary considerably in the frequency with which they would have a few contaminating staphylococci in the nose. This might account for the great differences in carriage rates, and the varying estimates of the increase in carriage among new nurses, which are given by workers who carried out single swab surveys. By including only those nurses who show true colonization of the nose as determined by three or four consecutive weekly examinations, this error is avoided. It seems likely that the high estimate of the increase in carriage in nurses entering the hospital environment has been accepted in much of the literature because the influence of occasional carriage has not been fully appreciated. Constant and intermittent carriers are probably the only ones of importance in disseminating staphylococci into the environment. Hare and Thomas[10] have shown that in intermittent carriers it is only when staphylococci are present in the nose that they are found on the skin and clothing, and that it is by way of these intermediate reservoirs and not from the nose directly that staphylococci reach the surroundings. The same is most probably true for occasional carriers and, since they have staphylococci in the nose for such short periods, they are probably not a source of appreciable staphylococcal contamination of their environment.

One of the most interesting findings in this survey has been the frequency with which nurses have acquired as their nasal colonizing strain, staphylococci of phage type 81 resistant to penicillin and tetracycline. The reason for this may be either that this strain has a particular capacity for colonizing the nasal mucosa, or simply that it is the one to which the nurses are most frequently exposed. The relatively rare occasions on which the strain was found only once without subsequent colonization, as compared with other resistant strains, tends to favour the hypothesis that it possesses a particular colonizing ability.

In this hospital, there has been a marked increase during the past five years in the incidence of staphylococci resistant to penicillin, streptomycin, and the tetracyclines, as has been reported elsewhere.[11] Phage typing of a series of these strains isolated in the last year showed that 85% were of type 81, and it is likely that most strains of this sensitivity pattern in earlier years were of this same type. Type 81 with this pattern of sensitivity has now become the most common strain in this hospital.

In 1956, Shaffer and his colleagues[12] reported an outbreak of staphylococcal infections in infants and nursing mothers in an obstetric hospital in Columbus, Ohio, due to strains of phage type 42B/47C/44A/52, and resistant to penicillin, streptomycin and chlortetracycline. These workers also found[13] that staphylococci causing

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epidemics of nursery infection in hospitals in other parts of Ohio, in Michigan, in Wisconsin, in Philadelphia and in Seattle, were all of this same type. Bynoe in Ottawa tested Shaffer's strains and found that, with his phages, they reacted as typical type 81 strains. He believes that these discrepancies are due to the wider range of activity of the American phages, and that strains reported in the U.S. as type 42B/47C/44A/52 are the same as those identified in Canada as 81.[14] There have been other reports from Texas[15] of an outbreak of sepsis due to a staphylococcus of phage type 42B/44A/81 and resistant to penicillin, streptomycin, and the tetracyclines, and from Cincinnati[16] of similar infections by a strain of phage type 42B/44A/47C/52/81 and resistant to the same antibiotics. These strains are probably the same as phage type 81.

In Australia[17, 18] and Britain[8, 19] very similar outbreaks of infection in hospitals have been reported due to staphylococci of phage type 80. There is considerable evidence[9, 14] to suggest that these are the same staphylococci as those classified in Canada as phage type 81. Gillespie and Alder[19] found that this penicillin-streptomycin-tetracycline resistant type 80 strain appeared readily to colonize the nose. This is in agreement with our belief that the resistant type 81 strain possesses a particular capacity for colonizing the nose, and that this may in part account for the rapidly increasing prevalence of the strain in hospitals in different parts of the world.

Why a strain which has been carried for months should be replaced by another, such as a resistant type 81, and why some people are consistent carriers and others non-carriers, are questions which require much further work for their elucidation. At present, the only means of dealing with carriers of strains causing cross-infection in hospital are local treatment of the carrier's nose with antiseptic or antibiotic creams, which is at best only temporarily effective, and by the general measures of nursing hygiene to prevent the transfer of carriers' staphylococci to patients. The solution of the basic problems of strain replacement and of the underlying causes of carriage and non-carriage may well be also the solution of the practical problem of the management of carriers of hospital cross-infecting staphylococci.

SUMMARY

Nasal carriage of *Staph. pyogenes* was investigated in 104 student nurses during the first eight to 18 months of their training and in 15 laboratory workers. The strains found were identified by their antibiotic sensitivity patterns and bacteriophage types.

The patterns of carriage in 51 nurses intensively studied were: true carriers—59%, consisting of 16% constant and 43% intermittent carriers; non-carriers and trivial carriers—41%, consisting of 35% occasional carriers and 6% non-carriers. The laboratory group showed similar patterns.

Only constant and intermittent carriers showed true carriage defined as consistent carriage of the same strain for several weeks. On this basis, there was no real change in carrier rates during the course of the survey even after exposure to ward environments. The true carrier rates remained between 30% and 40%.

During the survey there was a marked change in the types of staphylococci found in carriers. Strains fully sensitive to antibiotics, which were of various phage types, fell from 71% initially to 13% at 18 months. They were replaced by other strains, particularly by penicillin-tetracycline resistant phage type 81. This particular strain seemed more capable of colonizing the nose than others.

Staphylococci of phage type 81, resistant to penicillin and tetracycline, were frequently isolated from infected patients in the hospital.

A greater number of resistant staphylococci were picked up by the nurses on the surgical wards than on the medical wards and least on the isolation wards.

Preliminary experiments have failed indicate why non-carriers resist colonization and why some strains of staphylococci replace others in the nose.

We wish to express our gratitude to the nurses who took part in the survey and to the staff of the nursing school for their unfailing co-operation throughout the investigation, and to Dr. L. E. Elkerton, Director, Division of Laboratories, Ontario Department of Health, who most kindly extended to us the hospitality of his laboratory during the propagation of phage stocks and the typing of staphylococci.

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Résumé

Cent quatre étudiantes gardes-malades furent examinées pendant les premiers 8 à 18 mois de leur formation afin de découvrir la présence de staphylocoques pyogènes dans leurs fosses nasales. On examina de même 15 laborantines. Les souches furent divisées d'après le typage bactériophagique et la sensibilité aux antibiotiques. Cinquante-et-une élèves furent trouvées porteuses de germes. De ces porteuses chroniques, 16% hébergaient ces germes en permanence et 43% n'en gardaient que de temps en temps; 35% furent porteuses temporaires et rarement infectées. et aucun germe ne fut trouvé chez 6%. Des résultats semblables furent obtenus chez les techniciennes de laboratoire. Les porteuses constantes ou intermittentes seules ont répondu à la définition voulant que les mêmes souches de germes soient retrouvées chez les mêmes personnes pendant plusieurs semaines. A ce point de vue, on n'observa aucun changement dans la proportion de porteuses de germes pendant toute la période des recherches même après contact des malades dans les salles. La proportion des porteuses chroniques demeura entre 30% et 40%. Pendant le période de ces recherches on nota un changement considérable dans les souches de staphylocoques isolées chez ces porteuses. Les souches sensibles à tous les antibiotiques et de types bactériophagiques variés passèrent de 71% au début à 13% après 18 mois. Elles furent remplacées par d'autres souches résistantes à la tétracycline et particulièrement à la pénicilline, du type bactériophagique 81. Cette souche montra une facilité singulière à envahir les fosses nasales. A l'hôpital, ces mêmes souches furent souvent isolées de malades infectés. Les gardes-malades des salles chirurgicales portèrent un plus grand nombre de souches résistantes de staphylocoques que celles préposées aux salles médicales; les mieux protégées furent celles qui s'occupaient des cas d'isolement. On ne peut encore expliquer d'une part, la résistance des non porteuses à l'envahissement, et d'autre part, le remplacement de certaines souches de staphylocoques par d'autres souches dans les fosses nasales.

DIETHYLSTILBŒSTROL IN THE TREATMENT OF INOPERABLE CARCINOMA OF THE PROSTATE: A PRELIMINARY REPORT*

KENNETH J. MacKINNON, M.D., C.M., F.R.C.S.[C.],
T. N. NEARING, M.D., C.M., and
N. C. CARRUTHERS, M.D., *Montreal*

The initial work of Huggins on the use of œstrogens in the treatment of carcinoma of the prostate has led to the development and use of various œstrogenic substances in this disease. Their exact mode of action has not been established. It is possible that their effects result from action through the pituitary gland by inhibition of gonadotrophins, from action through the adrenal gland, or from direct action on prostatic tissue. It is also possible that their effects result from other mechanisms as yet unknown. The pituitary mechanism is the one commonly accepted. The purpose of this study is to attempt to evaluate the use of one of these œstrogenic substances, diethylstilbœstrol diphosphate, in the treatment of carcinoma of the prostate. This substance has been supplied to us in the form of Honvol.†

Honvol is a stable solution of the disodium salt of stilbœstrol diphosphate (diethylstilbœstrol diphosphate). It has been postulated that the administration of a high dosage of œstrogen with a target release mechanism might be more effective than standard oral œstrogens. In the past, this has been impossible in the absence of a water-soluble drug. The problem has been overcome by the introduction of the disodium salt of stilbœstrol diphosphate, an inert material permitting high dosage and intravenous administration. Theoretically, the active monophosphate of stilbœstrol is liberated through the enzymatic action of acid phosphatase in tissues rich in this substance. Therefore, it is reasonable to presume that in the prostate, and other tissues which are the site of metastases from the prostate, a high acid phosphatase content may break down the diphosphate to the active monophosphate and allow for cytotoxic action. Experimentally, this cytotoxic action has been demonstrated by Druckrey, Danneberg and Schmaehl[1]. It has recently been shown[2] that, shortly after the intravenous injection of Honvol into rats, a fairly high concentration of stilbœstrol is found in the prostatic tissue and this concentration is maintained for some time. It does not appear to affect acid phosphatase activity in the prostate of the rat.

Frajola, Muhsin and Taylor[3] reported some results of a series of 13 cases treated with

*From the Department of Urology, Royal Victoria Hospital, Montreal.
†Supplied by the Frank W. Horner Co. Ltd., Montreal.

diethylstilbœstrol diphosphate for carcinoma of the prostate. They observed a rapid clinical response involving relief of pain, euphoria and the absence of side effects. In those patients with elevated serum acid phosphatase, they noted return of these values to normal. They also noted initial rise in serum alkaline phosphatase, which later declined. Flocks *et al.*[4] reported a series of 66 patients treated with intravenous diethylstilbœstrol diphosphate for carcinoma of the prostate. They concluded that a significant percentage of their patients with advanced carcinoma of the prostate showed subjective and objective improvement from the use of this drug. Additional reports on the subject[5-11] record similar results. In nearly all cases, however, the side effect of burning or tingling in the perineal region and skin is reported, as opposed to the finding of no side effects by Frajola, Muhsin and Taylor.

At the Royal Victoria Hospital, 19 patients have been treated with the disodium salt of stilbœstrol diphosphate for inoperable carcinoma of the prostate. All received 500 mg. of the drug (daily by intravenous injection) for periods varying from 6 to 44 days. Six have died and 13 survive. The ages ranged from 53 to 81 years.

The patients' symptoms showed little variation. Twelve had symptoms of lower urinary tract obstruction (three of these had acute urinary retention), seven had bone pain in the back or hips, and four had hæmaturia. With one exception, the prostate felt stony hard and irregular.

On admission serum non-protein nitrogen (N.P.N.), and acid and alkaline phosphatase levels were determined. All patients had partial skeletal radiological surveys; of the 19, six had demonstrable metastases to bone. One patient had metastases to bone marrow as demonstrated in a marrow smear taken in the investigation of anæmia. Only four of the seven with metastases had bone pain, and these included the one case with malignant cells in the marrow smear. All but one of the 19 patients were considered clinically to have carcinoma; 15 were proven by biopsy. Included in these 15 was the one case in which the prostate was considered benign on rectal examination.

TABLE I.—Improved Cases

Case	*Age*		*Metastases to bone*	*Immediate results*	*Later treatment*
1.	61	Frequency, hæmaturia	None	Less frequency, hæmaturia stopped	Orchidectomy, T.U.P.R.
2.	81	Acute retention	None	Able to void with difficulty	T.U.P.R.
3.	71	Frequency	None	Less frequency	Oral œstrogens
4.	64	Leg pain, weight loss	Present	Pain disappeared	Oral œstrogens
5.	66	Back pain, leg weakness	Marrow	Less pain, general improvement	Oral œstrogens, orchidectomy
6.	79	Hip pain, nocturia	None	Less pain, less nocturia	Oral œstrogens
7.	59	Generalized pain	Present	Less pain	Nil
8.	64	Hip and back pain, general weakness	Present	Less pain, general improvement	Cortisone, orchidectomy

The long-term results of treatment could not be determined accurately because nearly all of these patients received other forms of therapy in addition to diethylstilbœstrol diphosphate. These included oral œstrogens, orchidectomy, and transurethral prostatic resection. However, the initial results of treatment were tabulated while the patients were in hospital.

Every patient experienced burning in the genito-anal region immediately on injection of the drug. Some experienced similar burning in areas topographically corresponding to underlying metastases. Others had generalized burning sensations. Some patients had nausea if the injection was given too rapidly, and one patient could not continue the medication because of persistent vomiting.

Eight patients experienced immediate relief of symptoms. Five had relief of bone pain, two had decrease of urinary frequency with a more forceful urinary stream, and one patient admitted in acute urinary retention was able to void with some difficulty. The remaining 11 were essentially unchanged and any subsequent improvement was attributed to either orchidectomy or transurethral prostatic resection (T.U.P.R.), with or without the use of oral œstrogens. The cases in which there was improvement are summarized in Table I.

Five of the patients had a decrease in serum acid phosphatase, and only three of these had elevated values initially.

Feminizing effects, such as are found with unphosphorylated œstrogens, were absent even in patients treated for some weeks. Following are case reports of three patients included in Table I.

Case 5.

M.G., a 66-year-old white male, was admitted on April 28, 1955, with complaints of weakness of the legs and pain in the back of one month's duration. His father, mother, a brother and a sister had died of carcinoma. Rectal examination revealed a moderately enlarged prostate with one hard nodule in the left lateral lobe. The serum acid phosphatase was 45.1 units (prostatic 31.9), and the alkaline phosphatase was 82.4 u. A bone marrow puncture was done for investigation of anæmia and neoplastic cells were found. There was no radiological evidence of metastases.

Diethylstilbœstrol diphosphate, in dosage of 500 mg. intravenously daily, was given. After 14 days of treatment the serum acid phosphatase was 4.2 u. (prostatic 2.0 u.) and the alkaline phosphatase was 168 u. There was immediate relief of pain and improved appetite. Treatment was continued for 19 days and the patient was discharged on diethylstilbœstrol diphosphate 500 mg. twice weekly. He was readmitted four months later. The serum acid phosphatase was 2.9 u. (prostatic 2.1 u.), and the alkaline phosphatase was 18 u. He was free of symptoms but continued to show malignant cells in the bone marrow, and it was felt that orchidectomy was indicated. The cells were not demonstrable after orchidectomy. This patient died 21 months after the beginning of treatment.

Case 7.

F.W., a 59-year-old white male, was admitted complaining of generalized bone pain of three years' duration. Transurethral prostatic resection had been performed for carcinoma three years previously and he had been treated with oral œstrogens since that time. After this, a bilateral orchidectomy was done. Bone pain persisted. Demerol was required frequently for pain. Later this patient had radiation therapy to the chest for secondary tumours. The pain persisted. On the present admission, the prostate was firm and fixed. The serum acid phosphatase was 7.5 u. (prostatic 4.3 u.), the alkaline phosphatase was 75.6 u. and the N.P.N. was 30.5 mg. %. Diethylstilbœstrol diphosphate therapy was started. Following the third dose, the pain had decreased but he still required Demerol. After the 14th dose the pain had further lessened and limb mobility had increased. The serum acid phosphatase was reduced to 5.38 u. (prostatic 3.54 u.) and the alkaline phosphatase was 81.7 u.

Case 8.

R.I., a 64-year-old white male, in the spring of 1955 developed severe pains in the lower back and hips. This was proven to be due to metastatic carcinoma of the prostate. He was treated with oral œstrogens with marked relief, for one year. In the summer of 1956, the symptoms recurred and he was admitted to hospital. On admission the serum acid phosphatase was 15.7 u. (prostatic 11.6 u.) and the alkaline phosphatase was 47.2 u. Diethylstilbœstrol diphosphate, 500 mg., was begun and given daily for 13 days. Following this, the acid phosphatase was 16.6 u. (prostatic 12.0 u.) and the alkaline phosphatase was 82.2 u. There was only slight remission of pain. The dosage was increased to 1000 mg. daily in 200 c.c. 5% glucose in water. This was continued for six days and resulted in relief of pain. After this, the acid phosphatase dropped to 2.5 u. (prostatic 0.2 u.) and the alkaline phosphatase was 40.2 u. Diethylstilbœstrol diphosphate was continued, 1000 mg. two to three times weekly, for two months. The pain recurred and the acid phosphatase increased to 20.0 u. Diethylstilbœstrol diphosphate was discontinued and cortisone begun. He later became refractory to this and was admitted to hospital for orchidectomy.

Other patients have received diethylstilbœstrol diphosphate for inoperable carcinoma of the prostate and the results of their initial treatment have closely paralleled the results of this group.

Conclusion

The intravenous use of diethylstilbœstrol diphosphate appears to be of some value in the treatment of inoperable prostatic carcinoma. It has been of definite value in at least two cases that became refractory to other forms of treatment, but the improvement was transitory. In practice, it is difficult to provide adequate therapy with this agent alone because these patients must return bi-weekly for injections and many are unable or unwilling to do this. It is because of this and the already proven benefits of other forms of therapy that we have not used this drug as an exclusive method of treatment.

Long-term and exclusive use of this agent is necessary to determine over-all efficacy in comparison with oral œstrogen therapy and/or orchidectomy.

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RÉSUMÉ

L'effet des œstrogènes dans le traitement hormonal du cancer de la prostate peut s'expliquer par leur action sur l'hypophyse en déprimant la sécrétion des gonadotropines. Les auteurs rapportent ici leur expérience dans l'emploi d'un composé hydrosoluble de biphosphate sodé de stilbestrol administré par voie intraveineuse (HONVOL, *marque déposée*). Ce produit assurerait une concentration d'œstrogène cytotoxique non seulement dans la glande elle-même, mais aussi dans les métastases. Dix-neuf malades furent ainsi traités à l'hôpital Royal Victoria de Montréal, à raison de 500 mg. par jour par voie intraveineuse pendant une période variant de 6 à 44 jours. Tous accusèrent une sensation de brûlement dans la région anogénitale ou aux environs des métastases. Plusieurs se plaignirent de nausées et l'on dut même interrompre le traitement chez un malade à cause de vomissements répétés. On observa une amélioration subjective immédiate chez huit malades; les onze autres ne semblèrent pas en retirer de bénéfice. En dépit des fortes doses on n'eut à déplorer aucun effet féminisant. Les faits cliniques de trois cas sont rapportés dans le texte.

APPENDICECTOMY: A CORRELATION OF THE PREOPERATIVE AND PATHOLOGICAL DIAGNOSES IN 1127 OPERATIONS

E. R. JUNKIN, M.D., *Calgary, Alta.*

INTRODUCTION

THIS IS A STATISTICAL SURVEY of appendicectomy, intentionally limited in scope, to provide an answer to the question "How accurately are we diagnosing acute appendicitis?"

The more significant question "What margin of error in the diagnosis of acute appendicitis is consistent with sound surgical practice?" requires further discussion, and a more detailed study of all aspects of the cases than is presented here. Previous papers have reviewed the results of appendicectomies performed at the Toronto East General Hospital, and the present study does not attempt to repeat such a review. The authors of these earlier papers, comparing the period from 1946 to 1952 with the earlier period from 1933 to 1939, suggested a correlation between a 10% increase in the proportion of operations performed for "clinically acute but pathologically not acute appendicitis" and a 10% decrease in the proportion of appendicitis with rupture. It was thought that this finding might be taken to indicate a trend towards earlier diagnosis and a willingness on the part of surgeons to operate earlier in acute abdominal conditions.

Ruptured appendix still carries a sixfold greater mortality than acute appendicitis with removal before rupture, in spite of the great over-all reduction in mortality. Therefore, the thought was expressed that with newly formed tissue committees in most hospitals it would be a retrogressive step if the removal of an uninflamed appendix was too readily criticized.

The material presented in the earlier reviews could not be analyzed for accuracy of diagnosis, and the present survey was undertaken to correlate preoperative and pathological diagnoses.

METHOD OF STUDY

At the Toronto East General Hospital a tissue committee has been functioning since May 1954. Without reference to the individual charts the reports to this committee were examined and information was tabulated with respect to all cases which showed: (a) a preoperative diagnosis mentioning appendicitis; (b) the removal of the appendix; or (c) a pathological diagnosis mentioning the appendix. These cases were divided into five groups according to the preoperative diagnosis:

"Acute appendicitis"—Acute appendicitis or any variation of this diagnosis provided the word "acute" was used.
"Appendiceal disease"—Any other diagnosis mentioning the appendix, not acute.
"Acute abdomen"—Any diagnosis suggesting an acute abdominal emergency but not mentioning the appendix.
"Incidental appendicectomy"—Any other preoperative diagnosis with apparently incidental removal of the appendix.
"Not recorded"—No preoperative diagnosis written on operative sheet.

The cases were also categorized with respect to the pathological diagnosis:

"Acute" included acute appendicitis and all variations, e.g. with gangrene, with perforations, and including acute periappendicitis.

"Not acute" included all diagnoses describing an abnormal appendix, not acutely inflamed, e.g. fibrosis, fæcalith, pinworm, tumour, sub-

*Read at a meeting of the Surgical Section of the Toronto Academy of Medicine on January 15, 1957.

acute, and periappendicitis without the qualifying adjective "acute".

"Normal" is self-explanatory.

RESULTS

In the 20-month period commencing May 1, 1954, and ending December 31, 1955, a total of 1127 appendicectomies were performed. Of these the preoperative diagnosis was missing in 182 (16.2%). Table I shows the cases grouped according to preoperative diagnoses.

TABLE I.

Preoperative diagnosis	*No. of cases*	*Pathological diagnosis*		
		Acute	*Not acute*	*Normal*
		(%)	(%)	(%)
Acute appendicitis	657	69.2	18.1	12.6
Appendiceal disease	136	13.2	57.4	29.4
Acute abdomen	24	45.0	30.0	25.0
Incidental appendicectomy	128	1.6	39.7	57.0
Not recorded	182	53.3	28.0	18.7
Totals	1127	51.8	27.2	21.0

Taking only the cases with a definite preoperative diagnosis of acute appendicitis, it can be seen that the diagnosis was confirmed in 69.2% of 657 cases, whereas in 12.6% the appendix showed no lesion and presumably was not concerned with the production of symptoms. This leaves 18% in which the pathological diagnosis was other than acute appendicitis but indicated some abnormality of the appendix. It is difficult to correlate such findings with the production of acute symptoms, and as a result considerable difference of opinion exists between various surgeons. Many would include all of these cases with the normal organs removed, and consider the diagnosis of acute appendicitis not confirmed. Other surgeons would insist that these findings indicate an abnormality which may well produce symptoms, even if not those of acute appendicitis, and feel that they should be kept separate from the other two groups. To avoid this area of disagreement it is thought that conclusions drawn from the figures shown for the other two groups only can be presented with some confidence.

In those cases where no preoperative diagnosis was available there is a significantly smaller proportion of pathologically acute appendicitis and it is probably not justifiable to consider that the preoperative diagnosis was missing because of some urgency in commencing the operation. Combining this group with that where a definite diagnosis of acute appendicitis was made would only reduce the proportion of cases with pathological confirmation while increasing somewhat the number of normal appendices removed; therefore the figures taken from the first line in the table give the best indication of the upper limits of diagnostic accuracy now prevailing as an average in this surgical department.

TABLE II.—ATTENDING SURGEONS ONLY

Preoperative diagnosis	*No. of cases*	*Pathological diagnosis*		
		Acute	*Not acute*	*Normal*
		(%)	(%)	(%)
Acute appendicitis	375	70.7	17.9	11.5

Where the diagnosis of appendiceal disease was made, 30% of appendices removed were normal, whereas 70% were abnormal and of these 13.2% of the whole group showed acute inflammation. When the totals for both acute appendicitis and other appendiceal disease are combined, the proportion of appendicitis pathologically acute is much lower, but the number of normal appendices in the combined groups amounts to only 15.5%, which might suggest an upper limit for this finding in all cases operated on for appendicitis.

Where other diagnoses of acute abdominal emergencies were made these included: "acute abdomen", "Meckel's diverticulitis?", ectopic pregnancy, intussusception, perforation of peptic ulcer, cholecystitis, peritonitis, and stab wound of abdomen. Under these circumstances only 24 appendices were removed; 45% of these were acutely inflamed. No particular conclusions are to be drawn from these figures, nor from those for incidental appendicectomy, although it is interesting to note that even in this group two cases (1.6%) showed acute appendicitis on pathological study. In both of these cases other more major procedures were carried out, thus justifying the inclusion of the cases with the incidental appendicectomies.

Restricting our view still further and considering only the cases where a preoperative diagnosis of acute appendicitis was recorded by one of the three attending general surgeons or by a member of the house staff operating under the supervision of these surgeons, the percentages in the pathological categories are shown in Table II to be within 1% of the figures for all operations performed in the department. The number of operations performed by miscel-

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laneous surgeons operating only occasionally at this hospital, and also by several of the senior general practitioners who have operating room privileges, amounted to about one-third as many as those performed by the attending staff. It will be noted from Table III that although more

TABLE III.—MISCELLANEOUS SURGEONS (OCCASIONAL OPERATORS) AND GENERAL PRACTITIONERS ONLY

		Pathological diagnosis		
Preoperative diagnosis	*No. of cases*	*Acute*	*Not acute*	*Normal*
		(%)	(%)	(%)
Acute appendicitis.....	126	61.9	21.4	16.7

operations were performed by this group for other than acute appendicitis, the difference is less than 10%.

Results for individual surgeons corresponded closely to the average for the department, with few exceptions. One individual has what appears to be a significantly greater proportion of cases of acute appendicitis pathologically confirmed than the average for the department or for any other individual. The significance of this fact is not apparent from the survey.

Several individuals with a percentage diagnostic accuracy far below the average had actually performed too few operations during the period for significance to be attached to these figures.

For a small time interval during the survey, it was possible to suggest whether the preoperative diagnosis and operation represented the work of one of the resident surgeons rather than that of the attending surgeon. As far as could be determined by the relatively small number of cases involving any one house surgeon, the percentages were similar to the average for the department. Certainly the total of all public ward cases would have little effect one way or the other on the figures for the attending staff. This statement is confirmed by the further similarity of the figures for the various surgeons who operated only on private patients.

It is not thought that the differential diagnosis of appendicitis is an important factor in the mistaken diagnosis of acute appendicitis; the reports showed other acute conditions present in only 31 (4.7%) of 657 cases diagnosed preoperatively as acute appendicitis, and this same number amounts to only 15.3% of the 202 cases in which the diagnosis was not confirmed by the pathologist.

SUMMARY AND CONCLUSIONS

Eleven hundred and twenty-seven operations in which the appendix was removed were studied for correlation between preoperative diagnosis and pathological diagnosis with respect to the appendix.

Where a preoperative diagnosis of acute appendicitis was made, pathological confirmation was obtained in 69.2% of 657 operations, and a normal appendix was removed in 12.6%.

These average figures for the entire surgical experience of the hospital were representative of the experience of most of the individual surgeons.

Where operation is performed for acute appendicitis, average diagnostic accuracy in this department approaches 70%, whereas if appendicectomy is performed for appendiceal disease, acuteness unspecified, the number of normal appendices amounts to no more than 16%. For cases where non-acute disease of the appendix is diagnosed preoperatively the accuracy is again 70%, the remaining 30% consisting of normal appendices.

In closing, I would like to express my gratitude to Dr. Burns Plewes, to the surgical staff of the Toronto East General Hospital, and to Dr. S. F. Penny, pathologist of that institution, for their help and constructive criticism. The assistance of Miss Margaret Morning, secretary of the tissue committee, in gathering the material was invaluable.

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1448A 17 Ave., S.W.,
Calgary.

RÉSUMÉ

L'auteur de cet article cherche à déterminer dans quelle mesure l'appendicite aiguë est diagnostiquée avec exactitude et jusqu'à quel point le chirurgien peut errer dans son diagnostic tout en intervenant sans nuire à son patient. Les risques fatals encourus par un malade sont six fois plus grands dans le cas d'appendicite suppurée que dans le cas d'appendicite aiguë sans perforation. Il ne faut done pas condamner trop sévèrement l'empressement du chirurgien à opérer. Au cours d'une période de 20 mois (1954 à 1955), 1,127 appendicectomies furent pratiquées à l'Hôpital Général de l'Est de Toronto. Le diagnostic d'appendicite aiguë fut confirmé à l'intervention dans 69.2% des cas alors que dans 12.6% l'organe ne portait aucune lésion pathologique. Une anomalie quelconque de l'appendice existait dans les autres 18%. Lorsque l'appendicectomie fut pratiquée pour maladie appendiculaire sans faire mention da la forme d'inflammation (aiguë ou chronique), le nombre d'appendices normaux réséqués ne s'élevait qu'à 16%. Les variations statistiques que peuvent entraîner les différents opérateurs (membres réguliers du département de chirurgie, omnipraticiens, internes, chirurgiens visiteurs, etc.) sont analysées aux tableaux II et III.

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THE PRACTICAL VALUE OF PHONOCARDIOGRAPHY*

ROBERT POTVIN, M.D.† and
DAVID STUBINGTON, M.B., F.R.C.P.[C.],
Toronto

DURING THE LAST DECADE the application of new techniques to the investigation of heart disease has led to a re-evaluation of many of the well-established physical signs. Phonocardiography, introduced over 50 years ago, has recently become a practical method and with its help many contributions to the understanding of heart sounds and murmurs have already been made.

While working in the Cardiovascular Unit of the Toronto General Hospital we have examined patients with interesting auscultatory findings with the help of phonocardiography. In most instances they were studied to elucidate a point which gave rise to difference of opinion at the bedside.

It is the purpose of this paper to describe the value and limitations of phonocardiography, using simple commercially available apparatus.

APPARATUS AND TECHNIQUES

A two-channel photographic recorder‡ was used for most of our work: this has several interchangeable bell and diaphragm chest pieces for attachment to an electromagnetic type of microphone. Logarithmic and stethoscopic curves of amplification are provided. With the logarithmic curve the true amplitude of low-pitched sounds is reduced, allowing the high-pitched ones to be shown more clearly. This curve resembles the response of the human ear. The "stethoscopic" curve gives an approximation to the sound *as delivered* by a standard stethoscope and has less attenuation of the low-pitched sounds. Using this, sounds below the threshold of human hearing can be recorded. The logarithmic curve was used unless especially low-pitched sounds or murmurs were sought. The paper speed was 75 mm. per second.

A direct-writing machine was also used.§ This is provided with galvanometers writing with a high-pressure ink jet. It has three frequency channels: high—200 to 800 cps., low—15 to 50 cps., and "aural", which resembles the logarithmic or human hearing curve. This is a very convenient machine to use but it does not produce records of as high quality as those from the photographic recorder.

As a reference tracing, standard lead 2 of the electrocardiogram was used routinely. When indicated, jugular or carotid pulses, using a Sanborn pulse pick-up, and occasionally intracardiac pressure pulses, were used as reference tracings.

The production of satisfactory records requires a relaxed, co-operative patient, who is not breathing heavily, a quiet room and a fair amount of time. The microphone should be held by hand or attached by suction: a rubber strap increases tension during inspiration and this changes the frequency response of the apparatus. Measurements are always made from and to the beginning of sounds, faint low-pitched components being ignored.

DISCUSSION

Heart Sounds

The phonocardiograph is of considerable value in the accurate identification of sounds and, in the lower frequencies particularly, it is often better than the human ear in the detection of faint sounds.

Split Sounds

Splitting of the first sound is common in health in young persons. It is best heard at the lower end of the sternum and at the apex. In the absence of bundle branch block it is rarely wider than 0.05 sec. A split first sound may be confused with the presystolic murmur of mitral stenosis. The phonocardiogram can decide this point by showing clearly that the murmur is present before the onset of the QRS complex of the electrocardiogram. Confusion is also commonly caused by the early systolic clicks resulting from dilatation of the great vessels: these are described later.

The second sound is caused mainly by closure of the semilunar valves. The aortic closes a moment before the pulmonary valve, but the sound produced is usually appreciated as single because the two components are very close. However, during inspiration there is increased venous return to the right heart, right ventricular systole is prolonged and the pulmonary element of the second sound is therefore delayed. At this time the sound can be appreciated as split in most normal individuals. In some persons, especially children, splitting can be detected at all phases of respiration. In expiration, the two elements do not usually commence more than 0.03 sec. apart, although the gap is occasionally as wide as 0.05 sec. in health.

It has been shown that the aortic element of the second sound is widely heard over the

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*From the Department of Medicine, University of Toronto, and the Medical Service, Toronto General Hospital. Part of this work was supported by a donation from Trinidad Leaseholds (Canada).
†R. S. McLaughlin Travelling Fellow.
‡Sanborn "twin-beam" Recorder.
§Mingograph, type 23: Elema Company of Sweden.

precordium, being well heard at the second left interspace and at the apex as well as in the classical aortic area. The pulmonary element is much fainter and is not usually detectable below the third interspace, unless there is pulmonary hypertension, when it may be louder than the aortic element and well heard over the whole precordium.

It will be seen, then, that the common teaching that the aortic sound is heard at the second right costal cartilage, and the pulmonary sound at the second left interspace, is not in accordance with the facts: both are heard at both sites and one must distinguish the two elements of the sound in order to compare the pressures in the two circulations.

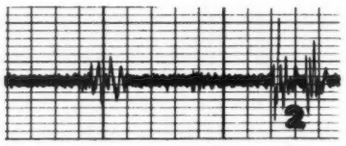

Fig. 1.—Wide splitting of the second sound in a case of atrial septal defect. Tracing taken in expiration over the third left interspace.
2 = split second sound.
Time lines of illustrations 0.04 sec. unless otherwise noted.

With atrial septal defects, the second sound in the pulmonary area is usually clearly split and in most cases the usual variation in the width of the split with respiration is lost. This splitting is consistently wide in atrial septal defects, unless there is pulmonary hypertension, when it tends to be close. Failure of the split to widen with respiration may also be found with anomalous pulmonary venous drainage—a condition physiologically similar to atrial septal defect. It should be emphasized that the splitting of the second sound alone does not allow the diagnosis of these conditions but it is of great value in calling attention to their possibility.

In pulmonary stenosis the second sound in the pulmonary area is widely split when the stenosis is of important degree, but the second element (pulmonary valve closure) is often very faint and in the most severe cases it may not be audible. Leatham has pointed out that there is a high degree of correlation between the right ventricular systolic pressure and the width of the splitting. These sounds can be recorded occasionally when they are not heard clinically.

In the tetralogy of Fallot only the aortic element of the second sound in the pulmonary area is usually heard.[1] Occasionally, however, a late faint pulmonary element may be heard or recorded. The tracings shown in Fig. 2 are from a case of Fallot's tetralogy diagnosed by catheterization and angiocardiography. The coincidence of the dicrotic notch of the aortic tracing with the first component of the split second sound shows that this is of aortic origin.

SYSTOLIC SOUNDS

Ejection Clicks

Attention has recently been focused on certain sounds which occur in early systole.[2] These short, high-pitched sounds have been described under various names: Lian wrote of them in 1937 as the "claquement protosystolique" and Wolferth and Margolies in 1940 believed that they were due to the opening of the pulmonary and aortic valves. They are probably best known as "ejection clicks" because synchronous pressure tracings have shown that they occur in the early phases of systolic ejection, and they are truly clicking in character. It is this very quality that makes them so distinctive.

The sounds are produced in the aorta or pulmonary artery when these vessels are dilated. Pulmonary ejection clicks are therefore found in pulmonary stenosis with post-stenotic dilatation, in idiopathic dilatation of the pulmonary artery and in pulmonary hypertension, irrespective of its etiology. Aortic ejection clicks are found in aortic stenosis, aortic incompetence, systemic hypertension, coarctation of the aorta and aneurysm of the ascending aorta.

As a rule the pulmonary clicks are best heard in the second left interspace, they are high-

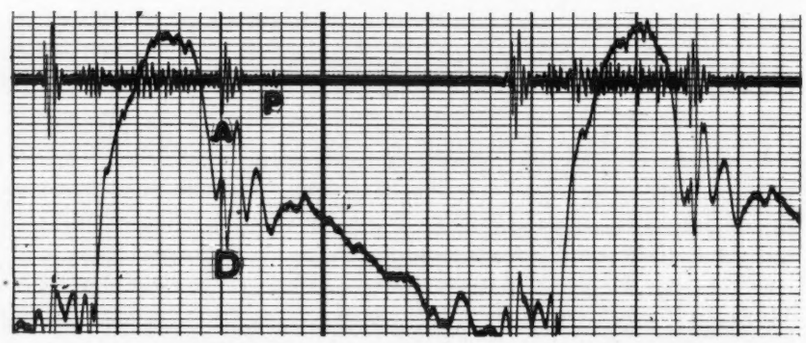

Fig. 2.—Tetralogy of Fallot: tracing from the second left interspace showing a faint delayed pulmonary element "P" after a normal aortic sound "A". Synchronous intra-aortic tracing obtained during right heart catheterization. The coincidence of the first component "A" of the second sound with the dicrotic notch "D" proves that it is aortic in origin.

pitched and short, show marked accentuation during expiration and are almost inaudible on inspiration. The aortic clicks are louder, well heard both at base and apex, and they do not usually exhibit the striking respiratory change of the pulmonary sounds.

For practical purposes a pulmonary click implies dilatation of the pulmonary artery. When present in mitral stenosis it indicates pulmonary hypertension and in cases with a left-to-right shunt it is usually associated with pulmonary hypertension. When there is pulmonary stenosis, it suggests post-stenotic dilatation and therefore favours valvular rather than infundibular stenosis but the sound is not heard when the stenosis is severe.

Pulmonary ejection sounds usually occur 0.05-0.08 sec. after the beginning of the first sound, but they may be seen between 0.02 and 0.14 sec. In the lower ranges, distinction from a split first sound may be difficult.

An aortic click is common in aortic stenosis. Its main importance lies in the fact that it may be misinterpreted as the first heart sound, and the first heart sound proper then called a presystolic gallop with the consequences implied by this observation. It can be difficult to make this distinction clinically, whereas it is easily made phonocardiographically.

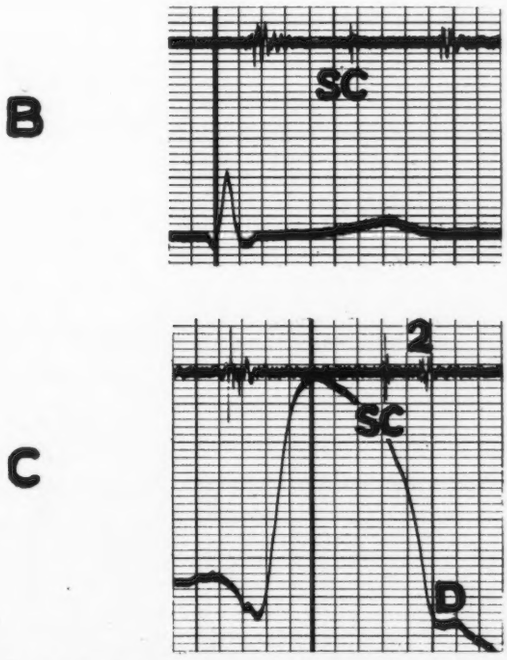

Fig. 3.—B: mid-systolic click in a case of atrial septal defect. Apical tracing before operation. After surgical closure of the defect the sound was no longer present.
SC = systolic click.
C: synchronous phonocardiogram and indirect carotid tracing. The clicking sound "SC" is in late systole, before the dicrotic notch of the pulse recording and its corresponding second sound.
2 = second sound.
D = dicrotic notch.

Mid and Late Systolic Sounds

Added sounds in these phases of the cardiac cycle are usually clicking in character but are occasionally low-pitched and deserving of the term "galop systolique" applied by Potain almost a century ago. Most commonly, no associated cardiac disease is found and in such cases Gallavardin's explanation that they are due to pericardial adhesions is usually given, but rarely confirmed. Occasionally such sounds are clearly related to a small pneumothorax, usually left-sided.

Clinically it is sometimes difficult to determine the exact position of these sounds in the cardiac cycle. The phonocardiogram may then be of valuable assistance.

Fig. 3B shows a mid-systolic click in a patient with an atrial septal defect. A fibrous band was found crossing a secundum type of defect and the sound was not present after closure.

Fig. 3C shows such a sound in a 40-year-old man with a story of ill-defined recent chest pain. There was no objective evidence of cardiac or respiratory disease, although chest films had not been taken in expiration to exclude a small pneumothorax.

Opening Snaps

The opening snap of the mitral valve is believed to be due to the sudden halting of the stenosed valve diaphragm as it moves into the ventricle in early diastole. This occurs at the moment when the intraventricular pressure falls below the intra-atrial pressure. It is found in almost all cases of mitral stenosis, provided that there is no great degree of calcification in the valve cusps or important regurgitation.

The opening snap is a short, high-pitched sound, which is best heard internal to the apex or in the lower sternal area. Respiration has little effect on its timing, but it is usually loudest in expiration. With tachycardia the left atrial pressure rises and the snap becomes closer to the second sound. The main difficulties are in distinguishing the sound from a widely split second sound and a third heart sound. The mitral opening snap usually has its onset between 0.07 and 0.1 sec. after the beginning of the aortic element of the second sound. Although the second element of a split second

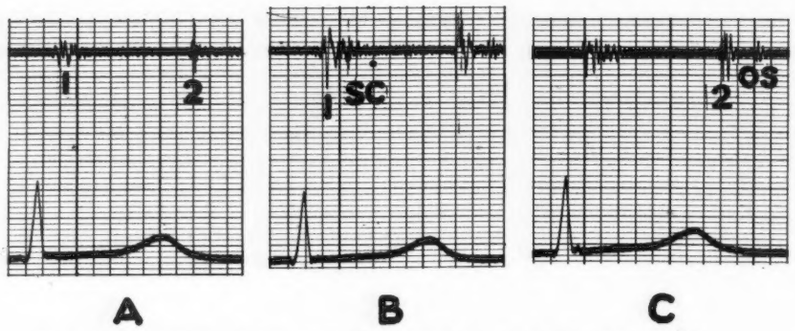

Fig. 4.—A: normal heart sounds at the base in inspiration.
B: early systolic click at the base on expiration.
C: opening snap well recorded at the lower end of the sternum.
From a case of mitral stenosis with pulmonary hypertension, the pulmonary arterial pressure being 70/40.
1 = first heart sound.
2 = second heart sound.
SC = early systolic click.
OS = opening snap.

sound may enter this time range in some normal persons during deep inspiration, the narrowing of the interval during expiration allows the distinction. The independent demonstration of both the split second sound and the opening snap recorded with two microphones synchronously offers the best method of clarifying this point.

Mounsey gives the range of opening snaps as 0.03-0.12 sec., but it is difficult to recognize the extremes with any certainty.

An opening snap originating at the tricuspid valve can sometimes be heard or recorded in tricuspid stenosis. The sound may be distinguished from a mitral snap (which is probably present also) by the demonstration of an increase in its intensity during the increased right-sided blood flow caused by deep inspiration. Fig. 5 shows such a case, which also demonstrates the increase in the intensity of the presystolic murmur with inspiration.

Bertrand Wells has observed that the nearer the opening snap to the second sound, and the greater the distance between the Q wave of the electrocardiogram and the first sound, the more severe is the degree of mitral stenosis. He has been able to estimate the diastolic gradient over the mitral valve with a fair degree of accuracy. We have found this to be true in several cases of tight pure stenosis.

The Third Heart Sound

This occurs in early diastole and is believed to be the result of vibration of the ventricular walls during the inrush of blood immediately after the opening of the atrioventricular valves. A normal third sound is commonly heard in healthy children and in young adults. The abnormal third heart sound is the so-called protodiastolic gallop.

The sound is low-pitched and as a rule is best heard at the apex or medial to it. It normally appears on the phonocardiogram beginning 0.14-0.16 sec. after the beginning of the second sound, but when the flow through the A-V valves is greatly increased, as in septal defects or gross mitral incompetence, it may be as early as 0.12 sec. The presence of the sound depends on the freedom of flow and it cannot therefore occur when there is any important

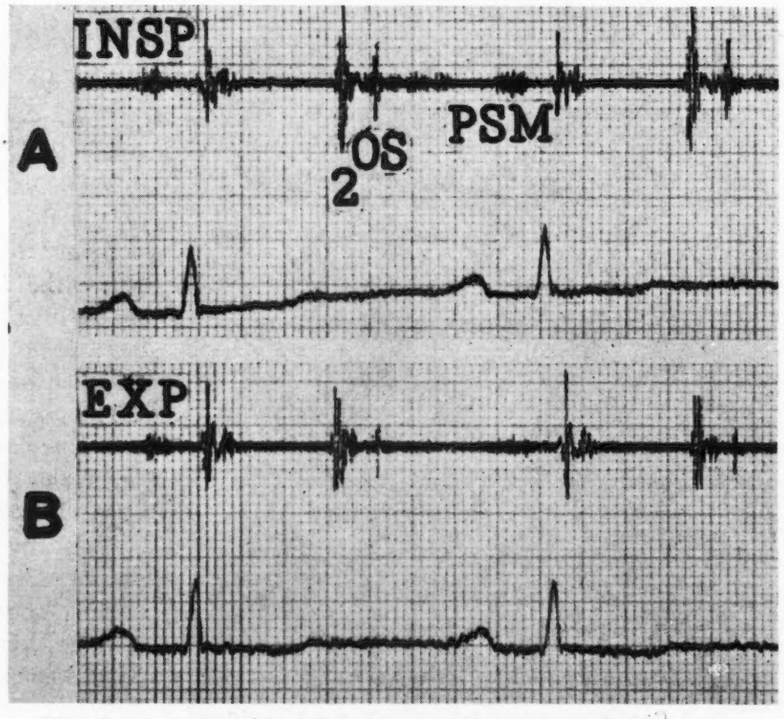

*Fig. 5.—A: lower end of the sternum after deep inspiration: an opening snap and a presystolic murmur "PSM" can be seen.
B: in expiration both are fainter.
Time lines at 0.02 sec.
From a case of tricuspid stenosis proven at operation.
*Retouched by the Medical Art Department.

degree of stenosis of the corresponding A-V valve.

In assessment of the relative importance of stenosis and incompetence in mitral valve disease, the third heart sound is a valuable indicator of a high degree of incompetence. It is known that an apical systolic murmur commonly occurs in the absence of a significant degree of incompetence, but it is not as widely appreciated that a mitral mid-diastolic murmur may be the result simply of a high degree of mitral incompetence, without significant stenosis. This latter murmur is often loud and may even be accompanied by a diastolic thrill, but it is always short, a feature that may only be appreciated when the heart rate is slow. It should be remembered also that the increased flow with septal defects may cause both a third heart sound and a mid-diastolic murmur of similar character, but the distinction will be made on other grounds.

Fig. 6 shows a tracing from a 22-year-old girl with rheumatic mitral valve disease. There was an apical diastolic thrill, an apical third heart sound and a mid-diastolic murmur which seemed to fill the diastolic period when the rate was fast, but which was clearly short when the rate was slow. There was no diastolic gradient over the mitral valve at left heart catheterization, indicating no important degree of stenosis. There were large prolonged systolic waves in the left atrial tracing, indicating a high degree of mitral regurgitation.

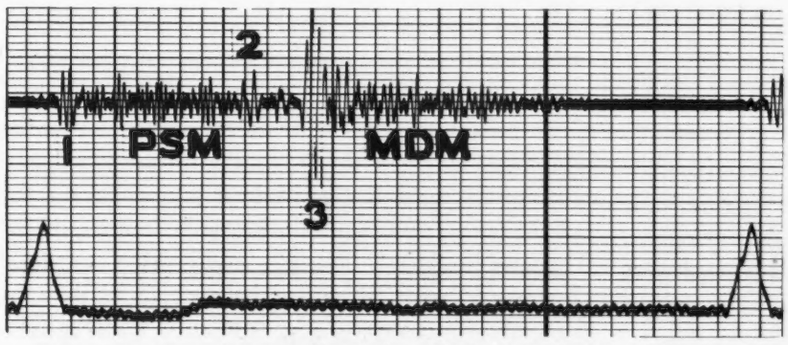

Fig. 6.—A case of pure rheumatic mitral incompetence. Apical tracing showing the typical pansystolic murmur of significant mitral incompetence "PSM", a loud third sound, and a short mid-diastolic murmur "MDM". Left heart catheterization showed no diastolic gradient across the mitral valve, excluding stenosis of any importance.
3 = third heart sound.

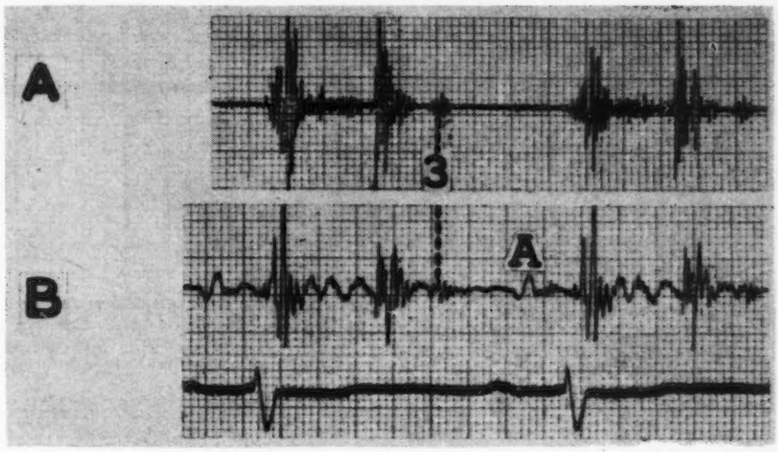

*Fig. 7.—Primary pulmonary hypertension; tracings from fifth space at left sternal border.
A: third heart sound; medium frequency channel.
B: auricular sound; low frequency channel.
A =auricular sound.
*Retouched by the Medical Art Department.

The Atrial or Fourth Sound

This sound is caused by the vibration of the ventricular walls during the inrush of blood from atrial systole. It is always abnormal when clinically audible. It is most commonly encountered as the presystolic gallop sound of left ventricular failure, but a right-sided atrial sound may be found in pulmonary hypertension and pulmonary stenosis.

The sound is low-pitched and is best heard in the lower left parasternal region or at the cardiac apex. It is recognized on the phonocardiogram by its occurrence before the onset of the QRS complex of the electrocardiogram and by the fact that it is best or only recognized in the stethoscopic or low frequency channel.

Fig. 7 is from a 45-year-old woman with primary pulmonary hypertension. An atrial gallop is well seen in the L.F. channel, and a third heart sound in both the aural and L.F. channels.

The Early Diastolic Sound of Constrictive Pericarditis

The majority of patients with constrictive pericarditis have an added sound in early diastole which is believed to be due to the sudden halting of rapid ventricular filling by the tight pericardium. This sound is snapping in character and may be loud or faint. It is best heard in the central precordium but is widely radiated

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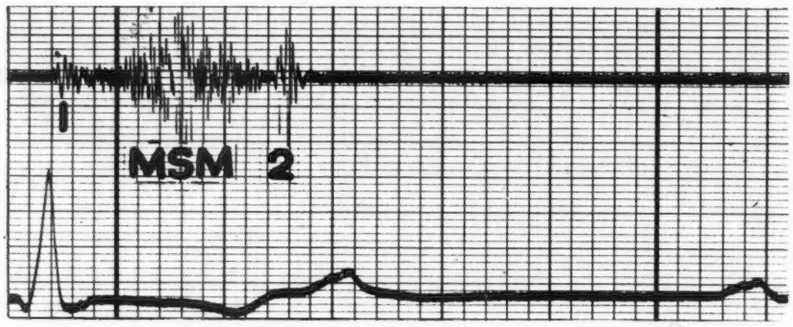

Fig. 8.—Aortic stenosis. Characteristic pattern: the murmur is mid-systolic and diamond-shaped. Compare with the murmur of mitral incompetence shown in Fig. 6.
MSM = Mid-systolic murmur.

when loud; it may be increased in intensity on inspiration.

The sound is valuable confirmatory evidence of the disease, although it may occasionally be absent. The value of phonocardiography lies in distinguishing it from a third heart sound and occasionally in detecting it when faint. Its timing is usually within the range of the opening snap.

MURMURS

Under ideal conditions, the faintest of murmurs can be recorded. Since such conditions are rarely attained, the phonocardiograph is not often helpful in deciding on the presence or absence of murmurs, but it is very valuable in assessing their configuration and length, from which important conclusions can often be drawn.

There are some situations where timing is difficult clinically; for instance, when there is tachycardia, or when sounds are faint. The phonocardiogram will always clearly show the exact situation of a murmur in the cardiac cycle.

The appearance of a given murmur on a graphic record depends greatly on the frequency response of the apparatus used; hence records from different workers can be compared only if details of the apparatus used are supplied.

The heart rate may also modify the appearance of a murmur. For example, the mitral diastolic murmur shown in Fig. 6 is relatively short; this suggests that there is no important degree of mitral stenosis, whereas a long murmur suggests more severe stenosis. The distinction could only be made when the heart rate was slow.

Basal Systolic Murmurs

The murmurs caused by obstruction to the blood flow through the pulmonary or aortic valves vary in intensity during systole with the pressure gradient across the valve. They are therefore usually crescendo-decrescendo, or diamond-shaped. The murmur of aortic stenosis has its main bulk in mid-systole, and it fades away to end clearly before the second sound. It has the same form wherever it is radiated. In valvular pulmonary stenosis the murmur is longer, passing up to, or even through, the aortic element of the second sound but ending before the faint, delayed pulmonary valve sound. Often the aortic sound is obscured by the murmur in these cases. With infundibular stenosis the obstruction is proximal to the pulmonary valve and the murmur may be earlier, ending before either component of the second sound.[3]

Apical Systolic Murmurs

Aortic systolic murmurs are frequently well radiated to the apex and they may then be difficult to distinguish clinically from mitral murmurs. The characteristic shape of the aortic murmurs in the phonocardiogram will usually allow this distinction to be made. The murmur of a high degree of mitral incompetence extends with about the same intensity through the length of systole: it is pan-systolic. Lesser degrees may be associated with shorter murmurs, but a diamond pattern is not seen.

Innocent Murmurs

The significance of a cardiovascular murmur must always be assessed in relation to the total clinical picture. However, long murmurs should always be suspect and a murmur extending clearly from first to second sound is almost certainly organic.

A particular variety of innocent murmur is the venous hum. This is a continuous murmur usually found at the root of the neck on the right side and sometimes well heard at the cardiac base. It is easily obliterated by light pressure over right jugular veins, or by the Valsalva manœuvre. Fig. 9B shows such a murmur in a 19-year-old-girl. Note that it shows diastolic accentuation unlike the continuous murmur of patent ductus arteriosus.

Diastolic Murmurs

In spite of their great importance in the assessment of valvular disease, we have rarely found the phonocardiograph of much practical value in this field.

On theoretical grounds the exact timing of the onset of an early diastolic murmur in relation to a split second sound should allow the distinction between pulmonary and aortic origin. However, although some workers have been more successful (Wells, Rappaport and Sprague, 1949),[4] we have found these murmurs very difficult to record, even when quite obvious to the ear.

Occasionally, as mentioned under "The Third Heart Sound", the phonocardiogram is helpful in deciding on the length of a mid-diastolic murmur.

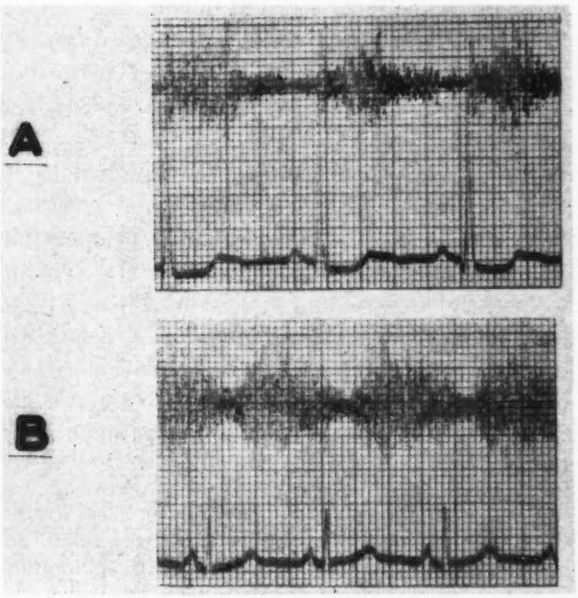

Fig. 9.—A: the murmur of patent ductus arteriosus showing accentuation in late systole.
B: innocent venous hum. The murmur is accentuated in diastole.

Continuous Murmurs

The murmur of patent ductus arteriosus usually shows accentuation in late systole, and the second sound is obscured by it (Fig. 9A).[5] Other conditions giving rise to a continuous murmur usually do not show this typical accentuation in late systole. These include arteriovenous fistula of the lung, rupture of a sinus of Valsalva, coronary arteriovenous fistula and the benign venous hum which at times can be well heard over the precordium. In a given case of patent ductus arteriosus, pulmonary hypertension should be suspected if the murmur does not show the typical pattern described above.

TEACHING

One cannot undertake phonocardiography diligently without being impressed with its value in teaching the art of auscultation. By providing an accurate and objective means of controlling one's observations it leads to increased awareness of the finer points of auscultation and to an increasing ability to utilize them.

SUMMARY

A study of the clinical usefulness of phonocardiography has been made.

The method is of great value in the accurate identification of heart sounds, normal and abnormal.

It allows the determination of the exact configuration and timing of murmurs and from these facts important conclusions can sometimes be drawn.

Perhaps its greatest value lies in teaching the art of auscultation.

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RÉSUMÉ

La phonocardiographie longtemps délaissée revient en usage grâce aux progrès de l'électronique. La sensibilité des appareils offerts dans le commerce en permet les applications les plus diverses; elle est surtout utile dans la perception des fréquences basses que l'oreille humaine ne saisit pas toujours clairement. La méthode est non seulement une aide indiscutable dans l'enseignement clinique et la formation sémiologique des étudiants, mais elle peut aussi apporter l'argument final à certaines discussions qui s'élèvent quelquefois entre cliniciens sur la présence de bruits adventices, leurs durées exactes et leurs positions dans le cycle cardiaque. Les auteurs commentent les tracés obtenus dans les cardiopathies courantes.

ANNULAR PANCREAS

Two cases of annular pancreas are reported by Boothroyd of Vancouver (*Am. Surg.*, 146: 139, 1957). The histories suggest pyloric stenosis or peptic ulcer, except that vomiting is frequent and relieves. The diagnosis is usually clear on careful radiological examination. Resection of the ring is often followed by fistula, and division of the ring may fail to relieve. Anastomosis of the proximal duodenum to the distal duodenum or gastro-jejunostomy is recommended in adults. In one of the cases, pancreatic ducts from the ring passed directly into the duodenum.

About 100 cases have been reported in the literature.

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SALVAGE RESECTIONS FOR PULMONARY TUBERCULOSIS*

GORDON W. THOMAS, M.D., F.A.C.S.,†
St. Anthony, Newfoundland

SINCE THE INTRODUCTION of chemotherapy, resection for pulmonary tuberculosis continues to offer more to an increasing number of patients. The surgical principles and indications for operation have been clearly laid down by early pioneers in this field.[1-4] The indications generally accepted for extirpative surgery have been: (1) failure of thoracoplasty, (2) persisting cavity, (3) empyema, (4) bronchostenosis, (5) destroyed lung, (6) bronchiectasis, (7) inspissated round lesion, and (8) residual necrotic focus.

As results have become more favourable, surgeons have become more aggressive and bolder in offering this type of definitive therapy to a wider group of patients. The advent of newer antibiotics promises some protection to those considered resistant to streptomycin, para-aminosalicylic acid (PAS) and isoniazid. Depending upon the type of case operated upon and the extent of surgery carried out, the end results reported as satisfactory vary in different series of cases from 70 to 90%, and reported mortality rates vary from 2 to 30%.[5-7] In reviewing the literature one is struck by these differences in mortality and cure rates in different series. In seeking the reason for this, it becomes readily apparent that these differences are directly related to the class of case operated upon and to the type of surgery carried out. The higher mortality and lower rate of cure are found, as one would naturally expect, in the patients with far advanced bilateral disease, who frequently have had everything else tried as well as multiple courses of several antibiotics, and whose operation must be considered as frankly salvage resections. These are apparently hopeless cases.

In carrying out 589 consecutive resections, Douglass *et al.*[5] report a cure rate of 70% and a mortality rate of 12% in those considered as salvage resections, in contrast to 95% well and 2% dead after elective procedures. Ottosen[7] reports on 20 salvage resections for thoracoplasty failure with a mortality rate of 30%. One immediately asks whether advising resection is justified in these cases, but when the otherwise hopeless outlook is considered one does not hesitate to do so.

Tuberculosis in Northern Newfoundland and Labrador continues to be our greatest single medical problem and, although it shows promising signs of coming under control and in line with other comparable areas of Canada, we still admit to our hospital many cases which would be classified by the National Tuberculosis Association as far advanced bilateral and in which any surgery must be considered a salvage operation.[8]

MATERIAL

This paper reviews 27 salvage resections in 25 cases, carried out in the Grenfell Hospital at St. Anthony, Newfoundland. One patient had bilateral resections, a right lower and middle lobectomy and a segmental resection of the posterior segment on the left side, and two others had thoracoplasty on one side and resection on the other.

The disease in all cases was classified as far advanced bilateral. We have not considered bilateral disease a contraindication to operation, and the following case illustrates the clearing frequently seen when a destroyed lung is removed and the focus which was constantly seeding tubercle bacilli taken away.

CASE 1.—A woman aged 27 was admitted in January 1952 with far advanced bilateral pulmonary tuberculosis. She had cough, night sweats, and weight loss for nine months before admission. On admission she weighed 100 lb., was toxic, and had a temperature of 102° F. Chest roentgenograms revealed far advanced fibroexudative and ulcerative infiltration in both lung fields with caseous pneumonia in the left upper lobe. Her sputum was positive for acid-fast bacilli on direct smear. Her case was felt to be hopeless but she was started on streptomycin and PAS.

She had been admitted in 1945 with a round lesion, probably inactive. A chest film in 1946 showed the same lesion, and the sputum at that time was said to be negative.

She showed marked clinical improvement after chemotherapy. She gained weight, her sputum diminished and she became non-toxic. The right lung showed signs of clearing, and after 11 months of chemotherapy it had cleared sufficiently for a salvage pneumonectomy to be done on the left side. At operation the left lung was found to be completely destroyed. The pathologist reported caseating tuberculosis with cavitation.

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*Presented at the annual meeting of the Canadian Tuberculosis Association, Niagara Falls, Ontario, May 17, 1956.
†The International Grenfell Association.

Postoperatively the patient did well. Her sputum converted to negative. She was discharged home for rest in June 1953, after 18 months of chemotherapy. At the time of discharge she weighed 132 lb.

She was followed up from time to time and remained well, doing her housework, until the spring of 1955 when she suddenly developed a severe respiratory infection which apparently was acute lobar pneumonia in her remaining lung. She died several days later. As she came from a fishing village where no medical aid was available, she was not seen or treated during this illness, and an autopsy was not done. She had had a check-up in our outpatient department several weeks before, however, and she was considered to be well with no apparent active disease.

This case illustrates the potential danger of a seemingly stable innocuous round lesion, as well as the clearing that sometimes takes place in apparently hopeless disease.

TABLE III.—PREVIOUS TREATMENT

	Drugs	*Other*
Pneumonectomy	6	6
Lobectomy	14	9
Segmental	3	3
Totals	23	18

courses of antibiotics and were considered resistant to two and frequently three drugs. Many also had other forms of therapy prior to resection such as pneumothorax, pneumoperitoneum or phrenic crush as well as prolonged bed rest (Table III). Twenty-three cases had at least one previous course of chemotherapy (some had multiple courses of three drugs); 18 had some prior definitive therapy. The following case illustrates what may be accomplished by salvage resection in a case having multiple courses of three drugs, as well as previous prolonged treatment.

TABLE I.—TYPES OF RESECTION

	Right		*Left*		*Total*
Pneumonectomy	1		6		7
	Lower	Mid	Upper	Lower	Upper	
Lobectomy	1	1	4	5	5	16
Segmental		1		2		3
Wedge				1		1
Total No. of operations		8		19		27

The types of resection carried out are shown in Table I. Nineteen operations were carried out in the left side, six of them pneumonectomies. Eight operations were done on the right side. Each of the three segmental resections was associated with a contralateral operation, in one case a lobectomy and in the other two a thoracoplasty. The wedge excision of a cavity was done at an attempted lobectomy for thoracoplasty failure that had to be terminated speedily because of insurmountable anæsthetic difficulties. This patient subsequently developed a bronchopleural fistula and empyema for which a pneumonectomy was done.

The indications for operation are shown in Table II. Most of our patients had had previous

TABLE II.—INDICATIONS FOR OPERATION

	Pneumonectomy	*Lobectomy*	*Segmental*	*Wedge*
Thoracoplasty failure	2	2	—	1
Destroyed lung	3	5	—	—
Residual cavity	—	8	3	—
Caseous pneumonia	2	1	—	—
Totals	7	16	3	1

CASE 2.—A woman aged 25 was transferred from another hospital in August 1954 with far advanced bilateral pulmonary tuberculosis. She had been treated off and on since 1949 and had multiple courses of streptomycin, PAS, and isoniazid. She was considered resistant to all three and had been turned down for any further procedures because of bilateral disease.

Chest roentgenograms showed the lesions on the right side to be undergoing some calcification. A large cavity was present at the left apex with an atelectatic left upper lobe. Sputum was positive for acid-fast bacilli. A left upper lobectomy was done several weeks after admission and followed later by a tailoring thoracoplasty. The patient was continued on all three drugs and was given terramycin postoperatively.

The pathologist reported ulcero-caseous tuberculosis of the lung with sequestration. After operation the patient did very well; her sputum converted immediately to negative. She gained weight and was discharged home to continue drugs as an outpatient in December 1954. She has remained well since. The lesions in the right lung have remained stable.

A favourable response after a salvage resection may be immediate and dramatic. This is

especially true when a destroyed lung or lobe is removed and unoxygenated blood no longer flows through an unaerated, functionless lung. The following case illustrates this.

CASE 3.—An Eskimo aged 30 was admitted in February 1955 acutely ill and toxic with far advanced bilateral pulmonary tuberculosis. Sputum was positive for acid-fast bacilli. The patient was dyspnœic, with an evening temperature to 104° F. Radiographs showed destroyed left lung with caseous pneumonia and a tension cavity 3 cm. in diameter at the right apex. She was started on Dinacrin (isoniazid), streptomycin, and PAS daily. She improved clinically but remained dyspnœic. The cavity at the right apex became smaller and the right lung improved although the left did not. She continued to have an evening elevation of temperature. A left pneumonectomy was done July 7, 1955, followed by a tailoring thoracoplasty. The pathologist reported ulcerocaseous tuberculosis of the left lung, endobronchial tuberculosis, and early sequestration of lung.

She improved immediately after operation. She was less dyspnœic and temperature fell to normal. Sputum converted to negative in September and has remained so since. Radiographs show the cavity at the right apex to have closed, and the right lung has remained stable. Sputum remains negative and the patient is now at full activity with no dyspnœa. She is being kept on long-term chemotherapy.

TABLE IV.—COMPLICATIONS

	Pneumonectomy	*Lobectomy*	*Segmental*	*Wedge*
Empyema	1	—	—	1
Spread of disease	1	3	—	—
Bronchopleural fistula	2	1	—	1

We have had 10 major complications in 27 operations (Table IV). Four of these complications directly caused the death of the patient. One was a massive breakdown of the bronchial stump in a pneumonectomy. The other three were due to progression of disease in the other side.

All other complications were handled satisfactorily, with the exception of one bronchopleural fistula which remains intermittently open after lobectomy for thoracoplasty failure. This patient is a respiratory cripple who would stand no further surgery.

The high rate of complications, 37%, after salvage operations is in line with those reported in other series of salvage resections.

Our experience in salvage resections for thoracoplasty failure has been poor. After four such resections one patient is dead, two still have active disease—both having developed bronchopleural fistula—and one is well with a satisfactory result and no apparent residual active disease.

TABLE V.—RESULTS

	No. cases	*Well*	*Still active*	*Died of T.B.*	*Died other cause*
Pneumonectomy	7	2	1	3	1
Lobectomy	16	12	3	1	—
Segmental	2	2	—	—	—
Totals	25	16	4	4	1

NOTE:—Where more than one operation was done, the case is classified under the more extensive procedure.

The over-all results are summarized in Table V. Of seven patients after pneumonectomy two are now well and one is alive on limited activity with a residual lesion in the opposite apex and an intermittently positive sputum. Four died of tuberculosis or of complications following surgery. Only one of these deaths was in the immediate (six weeks) postoperative period. Three were late deaths, 52 days to 18 months after operation. Another died three years after pneumonectomy of an intercurrent non-tuberculous infection (Case 1, above). Of 16 patients after lobectomy 12 remain alive and well. Three still have active disease, and on two of these we plan further contralateral operations in the near future. All patients who had segmental resections with contralateral surgery are alive, well, and working full time.

The over-all results show an early and late mortality rate due to tuberculosis of 16%; 68% were successfully rehabilitated; 16% still have active disease.

DISCUSSION

In our opinion it is worth while to offer resectional surgery to salvage cases whenever possible. When one considers the otherwise poor prognosis or the prospect of years of hospitalization as maximum benefit cases, a cure rate of 70% appears good. Overholt[9] has successfully carried out salvage resections for cavitary disease in patients with a single remaining lung. This type of surgery, although challenging, can be gratifying and we feel that it is justified.

There are certain important factors to consider in salvage operations. The first of these is the age of the patient. Our successful cases have all been

under 35 years of age. Our three unsuccessful resections for thoracoplasty failure were in older patients. Younger patients tolerate the trauma of operation better, make a quicker recovery, and show better compensation to alteration in pulmonary physiology. Secondly, the duration of disease is a factor. So-called "good chronics", those who have developed considerable resistance to the tubercle bacillus, will handle residual disease well once a residual cavity or destroyed lung from which bacilli are constantly being seeded is removed.

The side and extent of operation is important. Because the right lung is larger than the left, right pneumonectomy is not tolerated as well as left. More important than the side, however, is the degree of compensation which has taken place in the remaining good functioning lung; this can be easily tested by simple tests such as observation of dyspnœa on walking or going up stairs.

Nine of our salvage resections were on either Eskimo or Indian patients; their response to surgery was the same as in the white population. As a matter of fact, they tolerate surgery well, and only one of our deaths and unsuccessful results was in an Eskimo, the greater proportion being in white patients.

We believe resection offers more to salvage cases than other forms of therapy previously offered, such as cavernostomy, revision thoracoplasty, extrapleural pneumolysis, and the various types of plombage. The reason for this is that resection tends to conserve remaining functioning lung tissue while these others tend to reduce the function of remaining uninvolved lung segments.

Careful operative technique, adequate blood replacement, skilful anæsthesia with constant attention to a good airway during and after operation, and bronchoscopic aspiration of secretions postoperatively, all play an important part in successful surgery. We stress the importance of leaving in two intrapleural catheters after lobectomy, attached to a water seal bottle. We do not hesitate to leave them in for four or five days or longer when necessary.

SUMMARY

1. Pulmonary resection for tuberculosis offers much to salvage cases.

2. Twenty-seven salvage resections in 25 cases have been done at the Grenfell Hospital, St. Anthony, Newfoundland, with a cure rate of 68% and a mortality rate of 16%.

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RÉSUMÉ

Certaines interventions héroïques dans la chirurgie de la tuberculose sont entreprises comme dernier recours dans les cas désespérés. Il est ici question de 27 opérations dites "de récupération" pratiqués chez 25 malades tous atteints de tuberculose très avancée et bilatérale. La plupart d'entre eux avaient déjà acquis une résistance à deux ou même trois des antibiotiques employés dans ces cas, et plusieurs avaient déjà subi pneumothorax, pneumopéritoines, phrénicectomies, collapsothérapies en plus de longues periodes de cure. On compta dix complications sérieuses dont quatre entraînèrent la mort des malades (un moignon hilaire qui lâcha chez un pneumonectomisé, et l'extension progressive de la tuberculose gagna le côté opposé chez trois autres malades). Un opéré resta avec une fistule bronchique qui en fit un bon compte. Les résultats à date comprennent 68% de grand invalide respiratoire. Les autres s'en tirèrent à réhabilitation avec succès, 16% de tuberculose en activité et 16% de mortalité due à la tuberculose comme cause prochaine ou éloignée.

HEPATIC DERANGEMENT IN PULMONARY TUBERCULOSIS

One hundred cases of pulmonary tuberculosis in India were studied clinically, roentgenographically and bacteriologically by Sarin *et al.* (*Am. Rev. Tuberc.*, 76: 410, 1957). In addition, in each case a battery of liver function tests was performed along with biopsy studies.

Epithelioid cell tubercles with or without giant cells or caseation, or both, were found in 15 cases, one of tuberculoma. The liver was enlarged in 3 of the 15 cases, and hepatic function was moderately or markedly disturbed in 8 patients. Periportal lymphocytic infiltration was noted in 2 or 3 cases of miliary tuberculosis studied. Fatty infiltration, which is a common feature of tuberculosis, was seen in 27 of the 100 cases. It is believed to be due to the toxicity of the tuberculous infection, associated with malnutrition and metabolic disturbances.

Focal neurosis was common (47 of the cases). The necrosis is believed to be due to the toxicity of the tuberculosis in association with unidentified intestinal bacterial or protozoan infections which are quite common in India. Liver function was moderately or markedly deranged in 31 of the 100 cases.

It is possible that some of these findings may be due to the associated malnutrition, and might not be so frequently encountered in Western countries.

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Case Reports

CHRONIC IDIOPATHIC JAUNDICE WITH UNIDENTIFIED PIGMENT IN LIVER CELLS (DUBIN-JOHNSON SYNDROME)*

G. W. HALPENNY, M.D., C.M., F.R.C.P.[C.],
D. G. KINNEAR, M.D., C.M.† and
W. J. WHALEY, M.D., C.M., *Montreal*

THE OCCURRENCE of benign jaundice, coming on during youth or early adult age and persisting for many years in varying degrees, has been known since the turn of the present century when Gilbert[1] described a syndrome of familial nonhæmolytic jaundice. This syndrome has been variously termed Gilbert's disease or constitutional hyperbilirubinæmia by subsequent observers. Those afflicted with the malady complain of jaundice, lassitude, fatigability and vague dyspepsia, aggravated by stressful situations. Studies have shown normal liver morphology or early fatty metamorphosis and an elevated indirect van den Bergh reaction.

Recently a new clinicopathologic entity has been described by Dubin and Johnson[2] which can be distinguished from the original syndrome as described above. We have recently had the opportunity of studying such a case, the details of which are as follows:

A 24-year-old white man was admitted to the Montreal General Hospital on February 7, 1957, for investigation of a yellowish discoloration of the skin and eyes that had been present since childhood. He was contemplating marriage and was concerned about the prognosis of his condition. The patient stated that as long as he could remember his skin had had a yellowish tinge, his playmates frequently referring to him as "a little Chinaman". The degree of jaundice tended to wax and wane and during periods when it was most pronounced he noticed anorexia, easy fatigability, listlessness and dark urine, but denied fever, chills, pale stools or abdominal pain. Exacerbations, which occurred every 3-4 months and lasted 2-3 days, were not related to any obvious stress and in the intervening periods he felt perfectly well. There was no family history of jaundice.

In 1953 he was admitted to St. Bartholomew's Hospital in London, England, for investigation. His serum bilirubin was 4.3 mg. % with a strongly positive direct reaction. Further tests of parenchymal function, including a Takata Ara, thymol turbidity, zinc sulphate turbidity and total serum protein determination, were all negative. An obstructional element was ruled out by the finding of a normal alkaline phosphatase level and stercobilinogen excretion and there was no evidence of hæmolysis. A needle biopsy of the liver was performed, the pathological interpretation being similar to that of the specimen taken by us, as described below.

His past history was otherwise unremarkable and he had no symptoms referable to other organ systems.

On admission the patient, a normally developed and nourished young adult male, had obvious scleral icterus and a faint yellowish hue to the skin. The abdomen was soft and flat with no masses or areas of tenderness. The liver edge could not be felt with certainty but was felt to be enlarged two fingers'-breadths below the right costal margin by percussion. The spleen was not palpable and the remainder of the examination was within normal limits.

Urine was amber-coloured and contained 2+ bile. The hæmoglobin level measured 16.62 g. %, red cell volume 48%, sedimentation rate (Wintrobe) 5 mm. in one hour, white cell count 9400; differential—neutrophils 52%, lymphocytes 44%, monocytes 3%, and basophils 1%. Red cell fragility was normal, and the reticulocyte count less than 1%; blood platelets 230,000 per c.mm., and prothrombin time (Quick) 13 seconds. Serum bilirubin on admission was 1.4 mg. % (normal 0.1-0.2), one week later measuring 4.4 mg. %; a van den Bergh estimation done just before admission showed a direct value of 3.20 mg. % and an indirect of 4.60 mg. %. Fasting blood sugar 106 mg. %, blood urea nitrogen 10 mg. %, total proteins 6.5 g. % with an albumin of 4.0 and globulin of 2.5. Alkaline phosphatase 2 King-Armstrong units. Thymol turbidity one unit, cephalin flocculation negative, serum cholesterol 155 mg. %. A bromsulfalein test showed 20% dye retention after 45 minutes. Urine urobilinogen was 0.4 units per 100 c.c. and a direct and indirect Coombs test was negative. Only a very faint shadow was seen in the region of the gall-bladder following a double dose of oral contrast material.

A needle biopsy of the liver had been performed at St. Bartholomew's in 1953, the report being as follows: "Sections show very pale cytoplasm in the liver cells presumably due to a high glycogen content; there is also a marked pigmentation due to brown granules mostly in the central zone and situated in the liver cells themselves and in some of the Kupffer cells. A variety of histochemical stains has failed to reveal the nature of this brown pigment. It is not bile and there is no evidence of bile plugs in the canaliculi."

Liver biopsy was repeated on this admission, the pathologist reporting: "Sections reveal a small amount of liver tissue arranged in usual cell columns not including a total lobular structure and with no defined portal areas present. Fibrosis is not evident. The liver cells exhibit the usual fine cytoplasmic

*From the Department of Medicine, the Montreal General Hospital, Montreal, Quebec.
†Present address: 31 Pierce Rd., Watertown, Mass.

vacuolization indicative of a good content of glycogen and appear perfectly normal except that many of them contain an abundant pigment present in the form of finer and coarser granules with a green-brown colour reminiscent of biliary pigment. This is intracytoplasmic. There are no apparent bile thrombi in the canaliculi.

"The pigment seems to be contained only in the liver cells and is not present appreciably in the Kupffer cells. It does not give a positive Prussian blue reaction for hæmosiderin and likewise the Stein reaction for bile pigment is negative. The pigment resembles ceroid or lipochrome pigment but is coarser than these, and gives a negative acid-fast reaction with carbol-fuchsin. It is heavily stained by the Goltz modification of the PAS reaction."

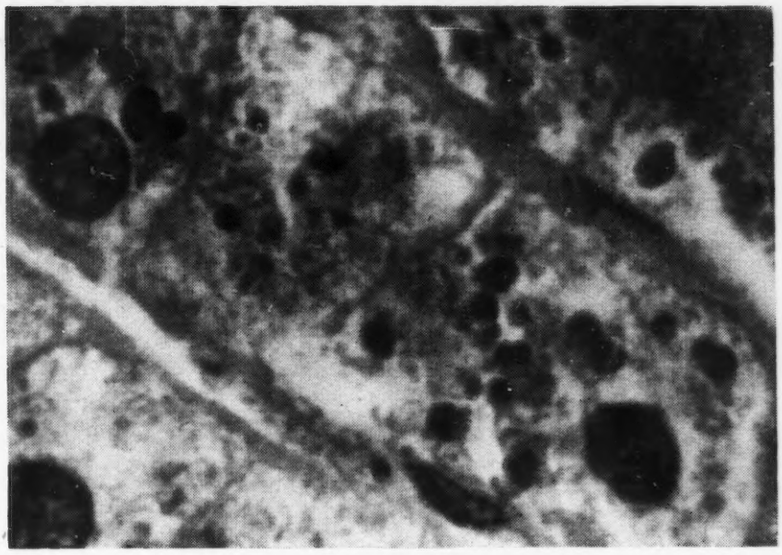

Fig. 1. × 24.

DISCUSSION

In 1954 Dubin and Johnson separated 12 cases of chronic intermittent jaundice which they felt formed a distinct entity. On the basis of laboratory investigation and liver biopsy they were able to show that their clinical material was similar to, yet clearly different from cases described by Gilbert as "simple familial cholæmia". This latter disorder has subsequently been referred to as "constitutional hyperbilirubinæmia" or Gilbert's disease. They pointed out that the following were relevant criteria in the differential diagnosis:

1. Presence of dark urine.
2. A higher incidence of bilirubinuria.
3. An increase in the direct van den Bergh reaction.
4. Occasional abnormal findings in liver function tests, e.g. alkaline phosphatase, cephalin flocculation and thymol turbidity.
5. Failure to visualize the gall-bladder on cholecystography.
6. Presence of coarse brownish pigmentation in liver parenchymal cells.

Several case reports[3-8] have appeared since Dubin and Johnson's monograph was published. We believe that our patient satisfies the above criteria and should be added to the growing list of cases comprising the syndrome "chronic intermittent jaundice with unidentified pigment in liver cells".

It is interesting to note that in most of the previously described cases the patient has suffered from varying degrees of abdominal pain. Our patient was completely free from pain. In addition, during periods of increased fatigability and lassitude, when his urine was darkest, he noticed that strenuous exercise such as cycling or a game of badminton would improve his sense of well-being. The explanation of this is not entirely clear. His illness in no way incapacitated him and he sought medical advice only to learn of the prognosis of his condition.

The essential procedure in establishing the diagnosis in this case, as in others, was the liver biopsy. The striking feature of the specimen was the presence of pigment as described above (Fig. 1). Several stains were used to elucidate the nature of this pigment but the classification of it remains obscure. Dubin and Johnson noted that it had certain histochemical properties in common with ceroid and lipochrome pigments. Brown and Shnitka[5] feel that it should be classed with the family of lipogenic pigments (lipofuscins).

The condition apparently has a benign course and the prognosis is good. The importance of attempting to classify cases of prolonged unexplained jaundice is at once apparent. Patients exhibiting the features of this syndrome can be confidently reassured. The etiology of this entity remains obscure. At present it is felt that it represents an inborn defect of the liver whereby such substances as bilirubin, bromsulfalein, and gall-bladder dyes are improperly excreted. A more precise explanation must await

further identification of the pigment found in the liver cells.

SUMMARY AND CONCLUSIONS

A case of the recently described clinico-pathological entity "chronic intermittent jaundice with unidentified pigment in liver cells" is presented.

The clinical picture and laboratory findings are outlined and emphasis is laid on the characteristic findings revealed by liver biopsy. It is noted that the syndrome can be separated from other cases of jaundice.

Features of the differential diagnosis are discussed. The course of the condition is benign, the prognosis good and the exact etiology obscure.

We wish to thank Dr. L. A. Caswell who kindly referred this case to us and St. Bartholomew's Hospital who forwarded their case summary. We are also indebted to Dr. W. H. Mathews of our Pathology Department for his work in interpreting the tissue sections.

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SEVERE SENSITIVITY REACTION (HEPATITIS, DERMATITIS AND PYREXIA) ATTRIBUTABLE TO PHENYLINDANEDIONE*

E. N. EAST, M.D., F.R.C.P.[C.], and
R. E. BEAMISH, M.D., F.R.C.P.[C.],
Winnipeg, Man.

THE VALUE of anticoagulant therapy in thromboembolic disease is now well established, but unfortunately the ideal anticoagulant has not yet been found. There are available a number of potent oral anticoagulant drugs which, by reducing prothrombin activity, successfully prevent thrombosis. However, undesirable side effects in the form of hæmorrhage or, less commonly, in the form of systemic reactions, may occur. Such reactions may constitute a greater danger to the patient than the disease for which the anticoagulant drug is being given.

*From the Department of Medicine, University of Manitoba, and the Department of Cardiology, The Manitoba Clinic, Winnipeg, Manitoba.

Of the oral anticoagulants in general use, we have found phenylindanedione (PID, phenindione, Danilone or Hedulin) to be most satisfactory.[1, 2] Because of the rapidity of onset of its effect, constancy of response in a given patient, freedom from hæmorrhagic and other complications, and response to antidote (vitamin K_1), it has recently been described as the drug of choice.[3-6] As it is likely that PID (phenylindanedione) will be used increasingly, it is considered desirable to report an instance of unusual sensitivity reaction observed to follow its administration.

The action of the coumarins and of the indanediones is to produce "hypoprothrombinæmia" by interfering with the ability of the liver to synthesize Factor VII and prothrombin. In view of this probable mode of action, it might be expected that toxic hepatic reactions would be common. Such has not proven to be the case. Wright, Marple and Beck[7] refer to an exaggerated response to dicoumarol in a patient with gross liver enlargement. They also state[8] that the effects of dicoumarol are unpredictable in the presence of hepatic dysfunction. For this reason, Barker[9] states that definite hepatic disease is a contraindication to the use of dicoumarol.

A survey of the literature reveals only one report of toxic hepatitis due to oral anticoagulants. Makous and VanderVeer[10] observed a severe sensitivity reaction with hepatitis, dermatitis, pyrexia, anæmia and leukæmoid blood picture in a patient treated with PID. A similar instance is here reported.

A 64-year-old white man was admitted to the Winnipeg General Hospital on May 4, 1955, with a three-day history of severe lower sternal and epigastric pain when walking. The pain came on after walking half a city block and disappeared after he rested for a few minutes. His past history included the passing of a renal calculus in 1934, repair of a right inguinal hernia in 1951, and in 1954 a diagnosis of gout for which no treatment was given. Physical examination on admission showed him to be moderately obese with a plethoric complexion. The heart sounds were normal, the blood pressure 165/95. There was no evidence of congestive heart failure. Abdominal examination was negative. The spleen was not palpable and there was no lymphadenopathy. An electrocardiogram showed terminal T wave inversion in V_3, V_4 and V_5 precordial leads. This was not present in a previous tracing in March 1954. Urinalysis and chest radiograph were negative. Examination of blood was as follows: hæmoglobin, 17.5 g. % (112%); red cell

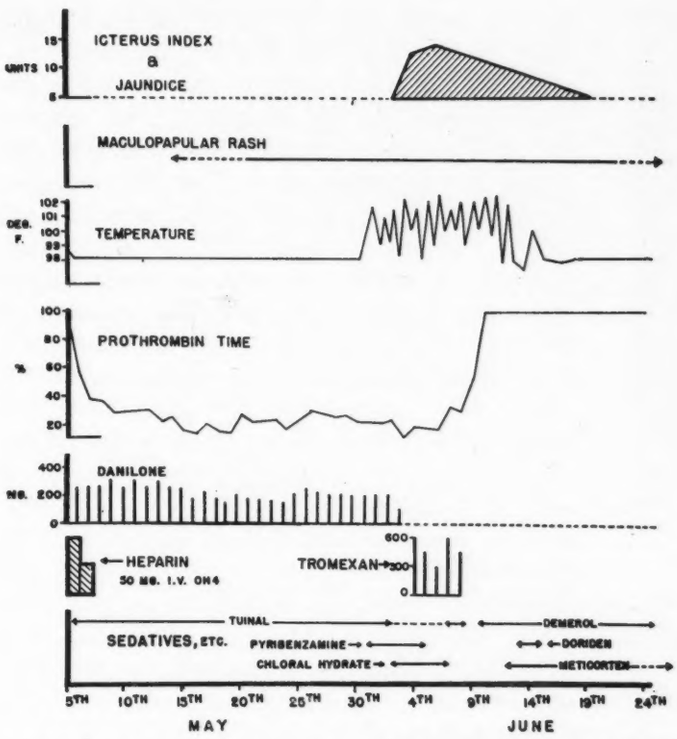

Fig. 1.—Hepatitis, dermatitis and fever attributable to phenylindanedione.

count, 6 million/c.mm.; white cell count, 10,500; differential count: neutrophils 54%, eosinophils 5%, lymphocytes 32%, monocytes 3%, atypical 4%; sedimentation rate 17 mm. per hour; icterus index, 5 units; prothrombin time 13.5 sec. (100%).

A diagnosis of angina pectoris with impending myocardial infarction was made and the patient was put at bed rest and given heparin, 50 mg. intravenously every 4 hours for 6 doses. Phenylindanedione (PID), 500 mg. in divided doses, was given the first day. The following day the patient had an episode of retrosternal pain with shortness of breath which was relieved with the sublingual use of 1/200 grain of nitroglycerin. On the third day a few fine rales were noted at both lung bases. The blood pressure varied during the first five days from 135/90 to 170/120. Serial electrocardiograms on May 5 and May 12 showed a lower T wave in lead I, inversion of T in AVL and increased inversion of T waves in V_2, V_3, V_4 and V_5. There were no QRS changes indicative of myocardial infarction.

For the first two weeks the patient had occasional attacks of chest pain which responded to nitroglycerin. The prothrombin time was maintained at between 25 sec. (36%) and 58.5 sec. (14%), with daily doses of PID averaging 223 mg. per day (Fig. 1).

On the 15th day a diffuse, itchy, erythematous macular eruption developed on the patient's back and upper abdomen (Fig. 2). This rapidly became generalized to involve the face and extremities as well. The intense pruritus did not respond to local applications or to drugs of the antihistamine group and continued unabated for the subsequent three weeks. The rash was diagnosed as dermatitis medicamentosa and barbiturate sedation was discontinued, but without effect on the pruritus or the eruption. Twenty-seven days after admission, 12 days after the onset of the rash, fever was noted for the first time, and on the 30th day, clinical jaundice was first seen. The liver margin became palpable 4 cm. below the right costal margin and was firm and non-tender. A maximum icterus index of 15 units was reported three days after the onset of jaundice. White cell count at this time was 8500 with 36% mature neutrophils, 21% young forms, 5% eosinophils, 2% basophils, 24% lymphocytes, 3% monocytes and 7% atypical lymphocytes. The erythrocyte sedimentation rate rose to 60 mm. per hour (previous maximum 38 mm.). The alkaline phosphatase was 19.2 King units. The cephalin flocculation was +++, thymol turbidity ++ and thymol flocculation 4 units. A stool specimen collected at this time proved negative for virus. Three weeks after the onset of jaundice the sedimentation rate was 40 mm. per hour, icterus index 5 units, white cell count 11,500 with no significant change in differential cell types, the Quick one-stage prothrombin time 15 sec. (90%); the absolute values of prothrombin and Factor VII (one-stage technique) were within normal limits. Factor V assay (one stage) was 40% of normal; this rose to 100% of normal two weeks later.

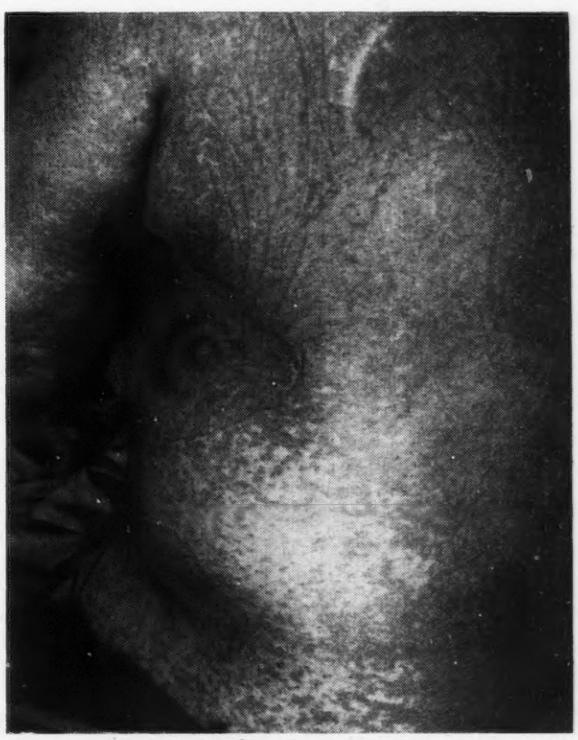

Fig. 2.—Erythematous macular eruption which appeared after administration of Danilone for 15 days.

On the 28th day of admission, 13 days after the onset of the rash, PID was discontinued and Tromexan substituted as an anticoagulant for five days and then it was also discontinued. The prothrombin time returned to normal within 48 hours. Jaundice, anorexia, rash and fever persisted unabated until the 39th day of hospitalization although the patient did not appear seriously ill. By this time the rash had been present for 24 days, daily afternoon fever to 102.5° F. for 12 days and jaundice for 9 days (Fig. 1). Meticorten (prednisone), 5 mg. t.i.d., was given orally, with improvement beginning the following day. A week later the rash had cleared completely and the liver margin was barely palpable. The patient's temperature remained normal after three days of Meticorten therapy. The subsequent course was uneventful and the patient was discharged on the 49th day. Meticorten was continued for 10 days after discharge, a total of three weeks, since considerable pruritus recurred when the dose was reduced before this.

DISCUSSION

There have been few reports of major or serious toxic reactions to PID in the literature and the incidence of these reactions certainly appears to be very low. Hæmorrhagic complications are considered to be due to overdosage or misuse of the drug or to a co-existent organic disease which has been ignored or unsuspected. Townsend *et al.*[11] report one patient who developed stomatitis and granulocytopenia while taking PID, with prompt recovery on withdrawal of the drug. MacMillan and Brown[12] noted two patients with agranulocytosis possibly due to PID, and Kirkeby[13] reports a case of agranulocytosis in which there was also a pruritic drug rash. The rash and blood picture improved dramatically with the use of cortisone although the patient died approximately three weeks later in uræmia, without definite cause of the latter being found.

This patient almost certainly suffered a severe sensitivity reaction. The consecutive development of a typical pruritic drug rash, with fever, anorexia and jaundice, strongly suggests a drug sensitivity. The rapid response of all symptoms and signs to Meticorten also favours this diagnosis. The only drug other than PID which could possibly be incriminated is the Tuinal (sodium secobarbital and amobarbital) given for sedation during the first 28 days in hospital. However, the patient had previously taken barbiturates without reaction and has subsequently taken them without untoward effect. In view of the history, course and laboratory evidence, other types of jaundice need not be considered.

In the only case report of toxic hepatitis due to PID found in the literature,[10] the reaction was very similar to that in the patient here described, but was more severe. This difference may have been due to the administration in their case of a second course of PID after the original reaction, at which time a leukæmoid reaction and anæmia also developed. The reaction in their case did not appear to respond as dramatically to corticotropin as did ours to prednisone.

Alexander[14] states that the drugs most frequently causing hypersensitivity hepatitis are the gold salts, phenurone and quinacrine, but others such as barbiturates, sulfonamides, and testosterone may do so. Clinical jaundice, with depressed hepatic function, is present but occasionally more serious hepatic necrosis may occur. According to Alexander, fever and skin eruptions commonly accompany the hepatitis, and immediate withdrawal of the offending drug is most important.

SUMMARY

A case history is presented of a toxic drug reaction to phenylindanedione. The patient developed, in order, pruritic rash, fever, hepatitis with jaundice. The rash was present for 12 days before fever developed; jaundice was apparent three days later and persisted for nine days. All the manifestations of hypersensitivity responded promptly to prednisone in small doses, although it was necessary to continue treatment for three weeks to prevent the recurrence of pruritus. References to other reports of toxic reactions to PID are discussed and the comparative rarity of these reactions is noted.

The authors are indebted to Dr. L. G. Israels and Dr. J. C. Wilt for hæmatological and virus studies on this patient.

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INTRATHORACIC LEIOMYOSARCOMA*

JOHN W. MERRITT, M.D., F.R.C.S.[C.] and
K. ROSS PARKER, M.D., *Halifax, N.S.*

INTRATHORACIC TUMOURS in children are always interesting diagnostic problems. Boyd[1] reviewed the 209 cases seen at the Toronto Hospital for Sick Children in the past 25 years and found that 49% of these were potentially malignant.

M.A.C., aged 8 years, was perfectly well during the summer of 1955. When she started school that fall her mother noted that she seemed more irritable than usual and that her appetite was falling off. She developed a dry, hacking cough with very little sputum, and her exercise tolerance decreased. She also seemed a little pale. She continued to go to school but lost a total of 30 days throughout the term. Up to this time she had not lost an appreciable amount of weight. Her general condition seemed to improve during the months of June and July 1956. In August she developed night sweats and began to complain of retrosternal pains. She also began to lose weight and to vomit, especially after the ingestion of heavy foods. On October 16, after some mild exertion, she experienced a bout of dyspnœa accompanied by wheezing and cough. Medical advice was sought, a radiograph was taken, and admission to the Halifax Children's Hospital was advised. Her past history was noncontributory except that there had been a recent contact with an active open case of pulmonary tuberculosis.

Physical examination: — She was a thin, pale, emaciated 8-year-old weighing 37½ lb. but in no acute distress. Small discrete glands were palpable in the cervical chain and also in axilla and groin. Chest expansion was limited in the left upper thorax. The trachea was deviated to the right. Breath sounds, tactile fremitus, and vocal fremitus were absent over the left upper thorax. The liver edge was palpable but not tender. The remainder of the physical examination was negative.

Investigation:—Vollmer patch test and test with intermediate strength purified protein derivative were negative. Urinalysis was negative, S.G. 1.003, Hb. value 7.65 g.%; white cell count 11,300; neutrophilis 70; band forms 1; lymphocytes 26; eosinophils 3; platelet count normal. Temperature on admission: 100° F. (oral). Chest radiograph (Fig. 1): Heart within normal limits. Right lung field clear. Heart, mediastinum and trachea displaced somewhat to the right by a circumscribed tumour involving the left upper lobe posteriorly to the mediastinum.

Total serum protein: 6.9 g.%. Alkaline phosphatase: 9.52 units. Cephalin cholesterol: 1+. Bilirubin: 0.42 mg.%, direct 0.2 mg.%, direct total 48%. Intravenous pyelography showed normal functioning kidneys. On bronchoscopic examination there was narrowing of the left main bronchus at the level of the upper lobe orifice. There appeared to be a greyish œdematous membrane or possibly tumour tissue, but several attempts at biopsy proved unsuccessful. Biopsy of cervical lymph node was negative for malignancy. Sputum (Papanicolaou stain) negative.

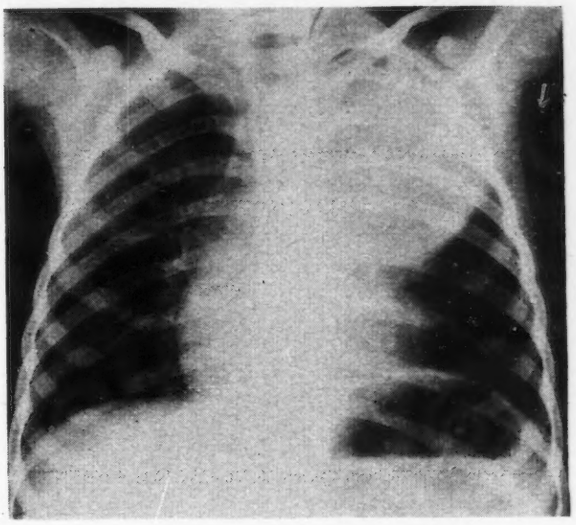

Fig. 1

The patient was given two transfusions of whole blood and a thoracotomy was performed on November 16. An intercostal incision was made in the 6th left intercostal space, and the tumour was found to be in the upper lobe, with the upper lobe compressed and reflected over the surface of the mass and largely airless. There appeared to be a line of cleavage between the lung and the tumour tissue. The upper lobe was so involved that its removal was necessary. Vessels were dissected, tied and ligated at the hilum and the bronchus was then divided and sutured. Specimens of lymph tissue were dissected from the hilum.

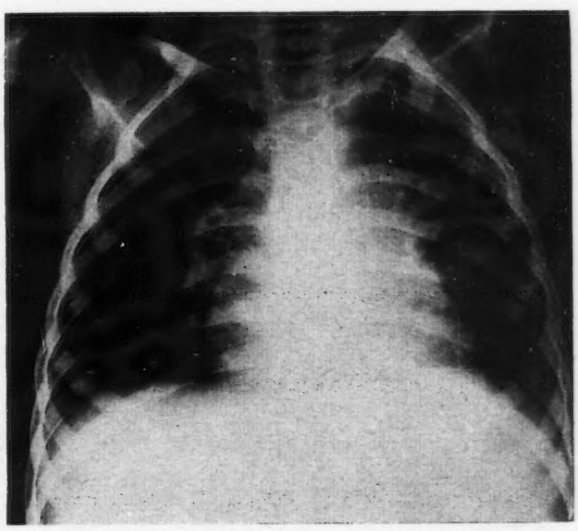

Fig. 2

*From the Department of Surgery, Halifax Children's Hospital.

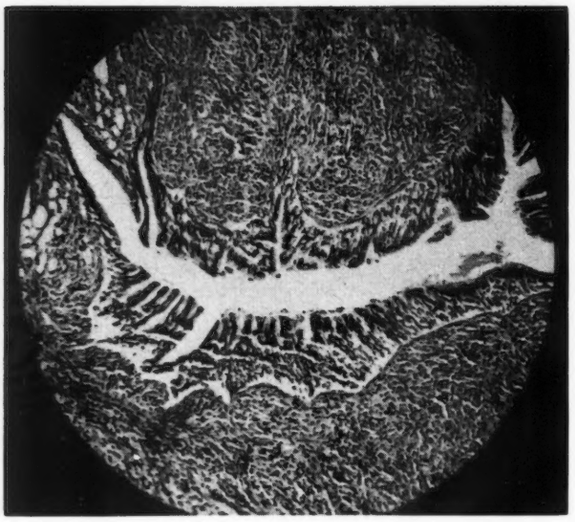

Fig. 3

The postoperative course was quite uneventful though a breakdown of the operation wound required treatment with antibiotics. The patient was discharged on December 3, weighing 39½ lb. and with a Hb. level of 10.2 g.%. Postoperative radiographs (Fig. 2) showed that the remainder of the lung field was well expanded, with no evidence of a lesion.

PATHOLOGICAL REPORT

(a) *Upper lobe of lung*: The apex was distended with a large solid oval mass, measuring 7 x 6 cm. The cut surface was slightly variegated. There were no areas of gross hæmorrhage; the texture was soft and fleshy; towards the inferior pole there were several irregular lightish-amber regions which cut with a gritty sensation. The lung lobe covered the tumour on the inferior and posterior aspects while a glistening membrane covered the superior portion.

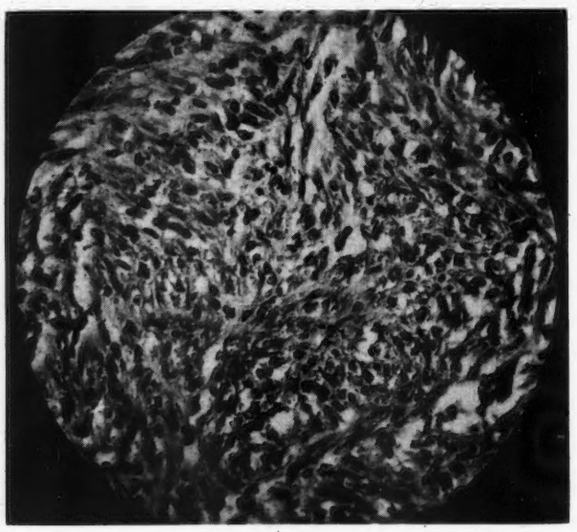

Fig. 4

Microscopic.—(a) (Figs. 3, 4 and 5) The tumour consisted solidly of tight whorls of elongated cells with abundant cytoplasm and oval nuclei. Special stains showed no collagen in the tumour although a capsule of collagen was formed at the upper pole by compressed lung tissue and pleura. On other surfaces the tumour was surrounded only by compressed lung tissue and the tumour cells seemed to infiltrate along the septa between alveoli. There was considerable lymphocytic infiltration through the tumour; several small bronchi were seen in the tumour and in one larger bronchus the tumour was polypoid. There were several areas of necrosis, some with patchy calcification, but no cytological evidence of frank malignancy in the form of aberrant nuclei or abnormal mitotic figures. (b) There was no tumour in the lymph node.

DISCUSSION

Most of the reported primary smooth muscle tumours of the lung have occurred in the older

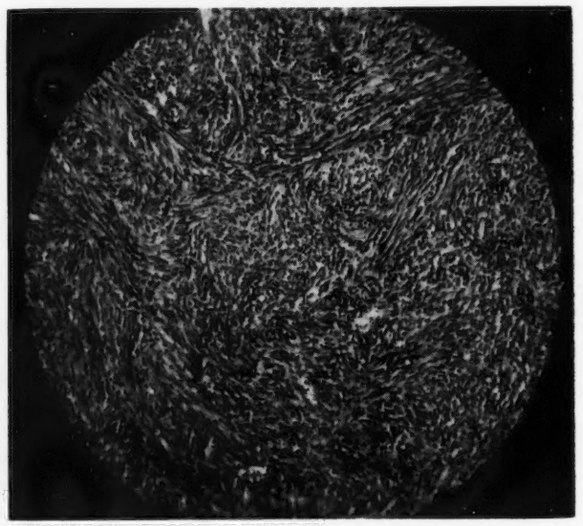

Fig. 5

age group (50-70) and are rare. In the literature, only 10 cases of leiomyosarcoma and 7 cases of benign leiomyoma have been reported and of these only two have occurred in persons under the age of 10. In 1954, Watson and Anlyan[2] reported an autopsy finding of a leiomyosarcoma in a 4-year-old boy, and in 1950, Williams and Daniel[3] reported a leiomyoma in an 8-year-old girl.

SUMMARY

A case of leiomyosarcoma of lung successfully treated by lobectomy is reported; this is the second such case reported in the literature in a child under the age of 16.

The authors are indebted to Dr. G. B. Wisewell, Physician-in-Chief, Children's Hospital, for permission to use the clinical material, and to Dr. W. A. Taylor, Provincial Pathologist, for permission to include photomicrographs (Figs. 3, 4 and 5) and the pathological report.

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TRICHOPHYTON RUBRUM INFECTIONS OF THE LOWER LEGS

P. TELNER, M.D., F.R.C.P.[C.],*
F. BLANK, Dr. sc. nat., Dr. sc. techn.† and
P. SCHOPFLOCHER, M.D.,* *Montreal*

INTRODUCTION

PRACTICALLY all cases of mycotic infection of the feet occurring in the Montreal area are caused either by *Trichophyton interdigitale* or *T. rubrum.*

An infection caused by *T. interdigitale* is usually characterized by acute symptoms, inflammation, vesiculo-pustular blisters, and trichophytid reactions, and gives a positive trichophytin test. The toenails are rarely infected. In the course of the last six years we have isolated this fungus only twice from toenails in which cases the fungal growth had been restricted to the surface of the nails. Infections due to *T. interdigitale* may easily be controlled by antimycotic treatment.

On the other hand, *T. rubrum* causes chronic, erythemato-squamous skin lesions, often accompanied by hyperkeratosis. If the infection persists for a long period, some or all toenails may become involved, appearing thickened, yellowish and brittle. *T. rubrum* infections of the feet are very hard to control, especially if the toenails, a steady source of infection and re-infection, are involved.

In contrast to infections caused by *T. interdigitale*, those due to *T. rubrum* have a tendency to spread to other parts of the body. In most cases of ringworm of the groin (eczema marginatum), a disease in former times exclusively caused by *Epidermophyton floccosum*, *T. rubrum* is isolated as the causative organism. Fingernails and palms of the hands become infected by scratching and rubbing other infected, itchy areas. We have also seen many cases in which this dermatophyte had infected the upper parts of the body, such as chest, back, beard and face. *T. rubrum* only rarely infects the scalp.

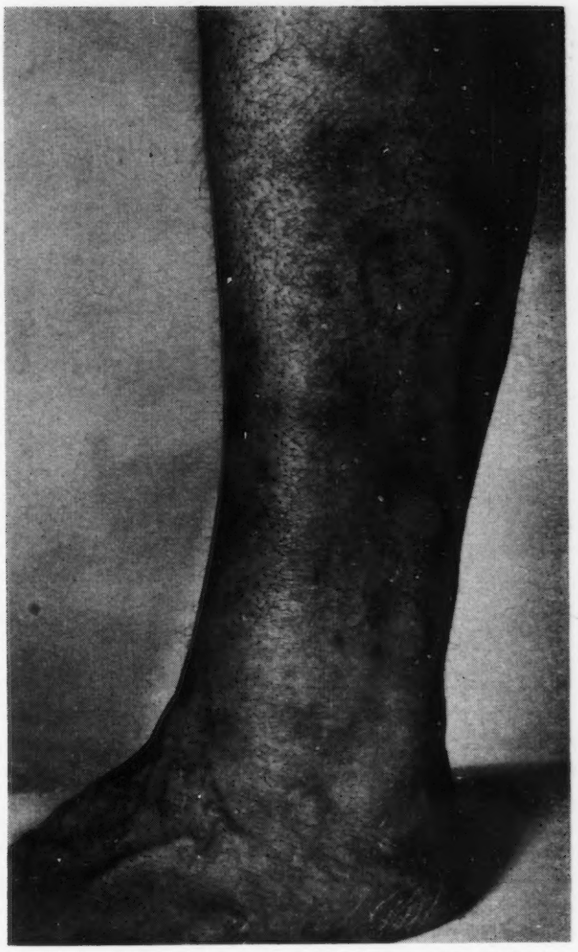

Fig. 1.—Nodular lesions and scaly dermatitis of the leg. Hyperkeratosis of the heel.

T. rubrum is a species which, from the mycological point of view, includes several varieties. Therefore, it is not surprising that so many types of lesions may be caused by this fungus. We wish to describe three cases of *T. rubrum* infections of the lower legs in order to draw attention to a clinical picture which is not uncommon. This clinical picture might easily be confused with other conditions such as superficial thrombophlebitis, nodular vasculitis, cellulitis of unknown origin and non-suppurative panniculitis.

CASE 1.—This 42-year-old woman first noticed a dryness and scaling of the soles of both feet about

*Royal Victoria Hospital, Department of Medicine, Sub-Department of Dermatology.
†Department of Bacteriology and Immunology, McGill University.

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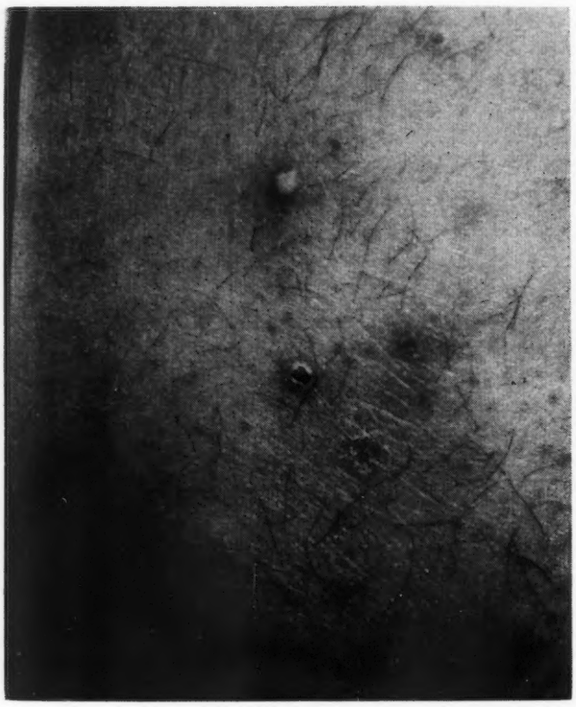

Fig. 2.—Pustular lesions and scar on the leg.

three years ago. Later, the nails became thickened, greyish and brittle. Painful nodules appeared on the posterior surface of the right leg. Similar nodules developed on the calf of the left leg. The nodular lesions remained unchanged for a number of weeks. Some of them disappeared spontaneously; others seemed to become more superficial. The overlying skin then became purplish and broke down, leaving a purple scar.

Occasionally a pustule was seen which contained a yellow, creamy pus not unlike that found in staphylococcal infections. The contents of such pustules were aspirated at two different times for culture. No aerobic or anaerobic bacteria were isolated, while a pure culture of *T. rubrum* was obtained in both instances.

The same dermatophyte was also grown from scrapings taken from the leg.

Sections of a biopsy specimen from the leg (involuting lesion) showed a moderate hyperkeratosis and a slight thickening of the stratum granulosum and the rete Malpighii. The upper cutis was œdematous and the capillaries were dilated. There was a mild diffuse cellular reaction composed of lymphocytes and fibrocytes with a sprinkling of polymorphonuclear leukocytes. The midcutis showed marked perivascular accumulations of lymphocytes. The periodic acid-Schiff reaction did not demonstrate any fungal elements.

Sections of a biopsy from a pustular lesion showed a relative hyperkeratosis covering a slightly acanthotic epidermis. A vesicle filled with polymorphonuclear leukocytes was situated intra-epidermally. The upper cutis contained a marked diffuse cellular reaction composed of lymphocytes, polymorphonuclear leukocytes and histiocytes. An occasional giant cell was present. In the midcutis the vessels were dilated and perivascular aggregations of acute inflammatory cells were found. In the lower part of the cutis similar cells surrounded the sweat glands. The periodic acid-Schiff reaction did not demonstrate any fungal elements.

CASE 2. – The patient, a 34-year-old woman, noticed a scaly dermatitis of the feet for some months, followed by the development of small pustules on the left leg. In addition, some deeply seated nodules were noted. At the time of examination she showed a follicular, scaly dermatitis but no actual pustules could be found. Dry pieces of scale were removed for mycological investigation. Direct examination of these scales showed septate hyphæ. Cultures of the scales grew *T. rubrum*, as did scrapings taken from the feet.

CASE 3.—The patient, a 44-year-old woman, gave a history of scaly dermatitis on the right palm in 1945 for which she received x-ray therapy. In 1951, nail changes were noted. *T. rubrum* was isolated from the nails in 1954. A scaly, itchy lesion developed on the leg in September 1954. The lesion extended at the periphery, formed a raised border and showed areas of healing in the centre. Scrapings were taken from this lesion and grew *T. rubrum*. Upon questioning, the patient remembered having received an insect bite on the site of the present lesion, which she had scratched with her infected fingernail.

Sections of a biopsy from the periphery of the lesion showed moderate hyperkeratosis. A nonspecific cellular reaction of lymphocytes and histiocytes was found in the cutis. Periodic acid-Schiff reaction showed many short and long septate hyphæ in the keratinous layer and a lesser number in the midcutis.

DISCUSSION

These cases were all seen within a short interval, and are believed to be more common than has been hitherto accepted, as a review of the literature will show.[1-3, 5, 9, 11, 12] Some reports[3, 9, 11] indicate that *T. interdigitale* may cause similar lesions on the legs as well.

Cremer[1] reported cases in which lanugo hairs of infected areas of the lower legs were invaded by *T. rubrum*. He also noted that this type of lesion tends to be unilateral but may become bilateral occasionally.

Wilson, Plunkett and Gregersen[12] drew attention to the fact that all their 14 cases occurred in dark-haired women. The same holds true for two of our cases. Both these women shaved their leg hair regularly. A period of pruritus followed shaving and they scratched the leg with their infected heels and soles. This could conceivably explain the location of the lesions

on the legs and the high incidence of such infections in dark-haired women. Scratching and insect bites have been thought for a long time to induce trichophytic granulomatous lesions.[4, 6-8]

It is most important to examine the feet and toenails as possible sources of infection of patients exhibiting lesions of this type on the lower legs. If possible, scrapings of skin and nails should be investigated for the presence of dermatophytes.

T. rubrum infections are well known to be recalcitrant to all forms of treatment. In two of our cases the application of fungistatic ointments on feet and legs combined with superficial x-ray therapy (Grenz rays) was followed by satisfactory clinical improvement.

SUMMARY

Three cases of nodular lesions associated with folliculitis and scaly dermatitis of the lower legs are reported. All three cases were caused by *Trichophyton rubrum*. The lesions of these patients were similar to those observed in cases of nodular vasculitis, thrombophlebitis or panniculitis.

The presence of such lesions on the lower legs should always lead to an examination of feet and toenails, with concomitant search for fungi in order to establish the diagnosis.

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AUTONOMIC NERVOUS SYSTEM

The autonomic nervous system is discussed in the latest issue of the *British Medical Bulletin* (Vol. 13, No. 3, September 1957). The approach to the problem is mainly along physiological lines. Those who, like Sir Henry Dale in the introduction, "wonder how many discoveries these relatively recent decades might have yielded in this field", would be well repaid by consulting this issue. An article on acetylcholine metabolism at nerve endings has been contributed by Professor F. C. MacIntosh and Dr. R. I. Birks, both of whom are on the staff of the Physiology Department, McGill University, Montreal.

SHORT COMMUNICATIONS

CLINICAL EVALUATION OF STEROSAN IN INFANTILE ECZEMA*

DE LA BROQUERIE FORTIER, M.D., F.A.A.P. and
YVES GREGOIRE, M.D., *Quebec, Que.*

IN SPITE OF THE RECENT availability of the adrenocorticosteroids, the problem of infantile dermatoses continues to give rise to numerous controversies along therapeutic lines. It is now generally acknowledged that this divergence of opinions may well explain the multiplicity of topical therapeutic methods, both physical and chemical, applied in the treatment of cutaneous lesions in childhood together with the conflicting results which they produce. Actual clinical observations on this subject are extensive but there is still a need for factual analyses of significance for medical evaluation; this indicates the lack of specificity and effectiveness of any of these surveys. Consequently there does not seem to be any alternative but to maintain a certain empirical approach to the problem. With this in mind, our attention has been directed to the study of a topical chemical agent in the treatment of either simple or complicated infantile eczema.

Preliminary research, to determine the fungistatic and bacteriostatic properties of certain derivatives of oxyquinoline in the treatment of pyodermatitis, was undertaken in Switzerland in 1944, under the direction of Jadassohn. Subsequent reports[1] proved that chlorquinaldol[2] was highly effective in a wide range of other skin disorders such as eczematous eruptions, psoriasis, impetigo, and other pyogenic dermatoses. Our clinical experiences during the period from February 1956 to January 1957 have prompted us to report 28 cases of infantile eczema treated in the pædiatric service directed by one of us (de la B.F.). Therapy consisted in local applications of chlorquinaldol, a 3% oxyquinoline derivative—more specifically, a 5, 7-dichloro-8-hydroxyquinaldine ointment in a petrolatum-beeswax base, known by the trade name "Sterosan".

CASE 1.—Daniel G., eight months old, had developed pruritic, indurated skin lesions on the face and extremities at the age of 2½ months. On preliminary examination, February 2, 1956, there was erythema involving both cheeks, the chin, the forehead and an area behind the ears. The lesions were partly covered with weeping, infected crusts, and the appearance of the scalp was such as to suggest seborrhœic dermatitis. Identical lesions were observed on the lower extremities.

*Pædiatric Service, Hôpital de l'Enfant Jésus, Quebec, Que.

On February 4, 1956, chlorquinaldol was applied freely to the affected parts. On February 6, the crusts had disappeared, and only moist erythema remained. Six days from the onset of treatment, the skin was soft and smooth, presenting a normal hue. Close inspection revealed only a few minute areas of erythema, distributed in the folds of the thighs and legs. The treatment was stopped, while the child remained under observation. After a mild attack of influenza, on February 20, 1956, there was a recurrence of the skin lesions, and chlorquinaldol was again applied. During this second course of treatment the regressive phase appeared to be more prolonged (eight days). Healing did occur, nevertheless, and the child left the hospital cured.

CASE 2.—Serge H., aged 2 years, was admitted to the pædiatric service on April 2, 1956, for an eczematoid dermatitis which had been present since the age of 6 months. Before chlorquinaldol applications, the child had presented with disseminated pruritic eruptions of the scalp and extremities. His face was covered with pustular and crusted lesions. The skin of the extremities was congested and oozed yellowish exudate. *Staphylococcus albus* was obtained on culture. On April 13, 1956, the skin showed reddish, lichenoid spots on the cheeks and post-auricular region, and circumscribed lesions on the lower extremities. There was no evidence of infection, however. After 15 days of treatment, there were still some brownish plaques scattered superficially on the inner aspects of the legs. The patient was permitted to leave the hospital on April 22, 1956.

CASE 3.—Claude L., 16 months old, was admitted to our service on May 7, 1956. Since the age of 9 months, the child had manifested impetiginous eczema with widespread distribution on the face, abdomen and extremities. These areas were intensely pruritic. Chlorquinaldol was prescribed, without any therapeutic adjunct. It was found to be effective in shortening the inflammatory phase. Itching diminished but was still present; and irritation due to scratching undoubtedly retarded the cure. On May 19, 1956, after an infection, the child's general condition deteriorated abruptly, and to hasten recovery, sulfonamide drugs were used. The sudden development of a wide-spread allergic pruritus compelled us to discontinue the use of this type of medication three days later. Chlorquinaldol was reapplied on June 1, 1956, on the cheeks and forehead, because a slight exacerbation of the eczematous lesions had been observed. The condition refused to heal and it was only with the aid of topical hydrocortisone that we succeeded in obtaining complete eradication of the disseminated indurated red patches on the lower extremities.

CASE 4.—Luc B., aged 5½ months, was placed under our supervision for furunculosis on the right occipito-parietal region on March 5, 1956. The skin of the rest of his body was red and dry; pruritus was intense. *Staphylococcus aureus* was cultured from the infected areas. Abscesses were incised with a scalpel and potassium permanganate dressings applied to the scalp. On March 14, 1956, examination revealed areas of pyodermatitis and superficial follicular pustules on the occipital region and lower extremities. Chlorquinaldol was then applied to the scalp, chest and legs. On March 19, 1956, papules and white scaly patches were still observed on the occipital region. Shortly thereafter healing was complete.

COMMENTS

In 28 cases of simple or complicated eczema, chlorquinaldol (Sterosan) was used from the onset of treatment, without any other medication. Clinical observations were made on children whose ages ranged from 1½ to 3 months; the duration of treatment extended over a period of two to three weeks. We noted that the majority of patients reacted favourably after the fifth day of treatment and that improvement was more rapid when the affected parts were covered with a thick layer of ointment. A protective dressing facilitated this procedure.

RESULTS OF TREATMENT

In this group, cures were obtained in 25% of cases and marked improvement in 64% of the group. Three children were only slightly improved. A single case of an allergic type of sensitization was encountered and this was attributed to sulfonamide therapy. Of the six recurrences, three reacted favourably to a second course of ointment. Cortisone was used locally for the other three cases (see Table I).

TABLE I.—RESULTS OF CHLORQUINALDOL THERAPY IN 28 CASES OF INFANTILE ECZEMA

Cures	7 (25%)
Marked improvement	18 (64.2%)
Slight improvement	3 (10.7%)
	28
Untoward reactions	0
Recurrences	6

SUMMARY

From these clinical observations it is our impression that chlorquinaldol is a potent bacteriostatic and fungistatic agent for topical use in infantile eczema. The medication should be intensive from the onset of treatment, and should be continued until there is complete disappearance of crusts and erythema.

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Special Article

TRANSFUSIONS ARE DANGEROUS*

BRUCE CHOWN, M.D., *Winnipeg, Man.*

AT LEAST HALF of all transfusions are unnecessary; personally I think the proportion is much higher than that. Every transfusion given to a girl or to a woman of child-bearing age carries a hidden threat, the threat of the death of her children. It does not matter how carefully the donor blood is selected, the threat remains.

Why do you transfuse? Why *do* you? Why do *you*? What is the proof that more than a small fraction of the blood that is daily poured into patients in the operating room alters the prognosis for the better? Blood has always had a mystical quality; its use in the operating room is more often mystical than scientific. And for women! Most transfusions given to women under the age of 45 are given in relation to pregnancy—for the bleeding associated with an abortion, with a vaginal delivery, with Cæsarean section—even, God save the mark, for simple anæmia. I would hazard the guess that not 5%—no, not 1%—of transfusions so given have been life-saving. And I would hazard the guess too that at least as great a percentage has been death-dealing.

Death holds his cards close to his belly, and he plays them slowly; sometimes very slowly. So you forget. Or you don't know; you're no longer in the game when Death plays his trump. Let me tell you a story.

One day in 1951 Mrs. Schmaltz, let us call her, then three months gone in her third pregnancy, went to bed feeling well. In the night she woke to find her waters had broken, and early next morning she delivered herself of a fetus. For a day and a night she bled at home; then she went to the hospital. She was pale; her hæmoglobin was not measured. She was no longer bleeding. Next day towards noon she was taken to the operating room, curetted and, while still under the anæsthetic, given a transfusion. (Luck was with the operator; she didn't have a reaction.) Next day she felt fine and was given another transfusion, and a few days later she went home. Death played his trump card five years later when a baby was born to Mrs. Schmaltz with erythroblastosis, from which it died before it could be transfused. The erythroblastosis was not due to the Rh factor or to any of its kith or kin but to an entirely unrelated blood group system.

The most careful selection of the donor blood under our present methods of selection would not have prevented the sensitization of the mother and the sequent death of the baby. And in this case there was no question of saving the mother's life; she was never in danger; the first transfusion was not given until 30 hours after admission to hospital and at least as long after bleeding had stopped; the second transfusion was given for no apparent reason. The giving of transfusions seems to be a conditioned reflex: abortion, transfusion; abortion, transfusion. So it goes. But why? Why? Let me tell you another story.

A 31-year-old woman was admitted to hospital in March 1954, suffering from an incomplete abortion.[1] She was of a rare blood group, and, having had eight transfusions in connection with earlier abortions, had developed antibodies which reacted with the blood of almost all potential donors. While compatible blood was being sought, her blood pressure fell to 70/50 mm. Hg, her hæmoglobin from 8.5 to 5.8 g. per 100 ml. (from about 60 to about 35%). A compatible donor was found at last, but the patient had such a severe pyrogen reaction to the transfusion that it had to be stopped when 250 ml. had been given. No further transfusion was attempted: *her hæmoglobin was 14 grams per 100 ml. within a month.*

I tell you that story before you say to me about Mrs. Schmaltz, "It may not have been necessary to the saving of her life, but it shortened her convalescence." Did it? By how much? A week? Two weeks? Three weeks? Certainly with a bit of iron her hæmoglobin would have been up to normal within a month. And would she willingly have traded her baby's life for those few draggy weeks? Mrs. Schmaltz had changed doctors between 1951 and 1956, so the transfuser of 1951 never knew about the bad result of his "good" treatment.

I'll tell you some other stories another time.

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*From the Rh Laboratory, 735 Notre Dame Ave., Winnipeg 3, and the Department of Pædiatrics, University of Manitoba.
This is the first of three articles.

INFLAMMATIONS OF THE NON-LACTATION BREAST

Infectious mastitis, tuberculosis, chemical mastitis, traumatic mastitis, inflammatory carcinoma of the breast, chronic cystic mastitis and scleroderma are reviewed by Pratt (*Am. J. Obst. & Gynec.*, 74: 844, 1957). Anything that threatens to mar or sacrifice the evidence of femininity is a justifiable cause for anxiety. The significance of the anxiety is not always appreciated by the physician, although it is very important to the patient. Thoughtfulness in diagnosis and conservation in treatment will earn the gratitude of the patient.

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SOCIO-MEDICAL CARE OF THE ELDERLY

With the continuing forward march of medical knowledge, more and more members of our society are outliving the perils of youth and middle age and entering the ranks of the elderly. In a society that has not foreseen this development, and has therefore failed to make appropriate provisions for its results, the community is being presented with problems both real and imagined, some of which demand urgent consideration and planning for the future.

In an attempt to divorce fact from fancy and desire from necessity, a thoughtful British general practitioner has made a study[1] of this problem which should most certainly place matters in their proper perspective and allay unnecessary fears and worries. While it is undesirable and unnecessary to quote his findings in statistical detail, a few of his conclusions are most refreshing and are distinctly worthy of citation. Contrary to popular opinion, one does not automatically at the age of 70 give up all interest in life and of necessity become a burden to the family or to the state. Many people in this age-group can work and do work, either gainfully in industry or in their own businesses; at very least they are able to take care of their own homes and persons.

Only about 10% of men or women aged 70 and older require *permanent* care in hospitals or homes for the aged. Most still live with their families, and a smaller proportion with their spouses or by themselves.

The problem of physical, mental or "social" disability in the aged also receives careful consideration in this study. For many years, rigid criteria for the term "disability" apparently dictated by industry have resulted in gross and unnecessary errors of placement and management. The question of disability should be dealt with in terms of "effective function". By this usage, only 35-40% of people from 70 to 80 plus are sufficiently disabled for their daily routine to be interfered with.

As regards outside diversion, so-called "senior citizens' clubs" are extremely useful and are becoming more and more widely available, but are not being utilized widely enough.

From the purely medical point of view, it is salutary to note that the term "geriatrics" does not appear once in the entire study. There are no diseases peculiar to old age, and it is to be hoped that the present downward trend in popularity of this pseudospecialty will continue and be accelerated. Many of the disabilities encountered in old age are improvable or curable or both by routine medical or surgical means. Elderly patients with coughs are no longer being passed off with a diagnosis of "bronchitis". Many are being found to have tuberculosis and are being successfully treated in our sanatoria, where they are having interesting effects on the age-statistics. "Heart failure" in the elderly frequently has a cause that can be removed; or if not, the failure itself can be intelligently treated. Dietary neglect with multiple vitamin deficiencies is readily correctible. The techniques of surgery and anæsthesia have improved so radically that if operation is required advanced age is no longer a contraindication.

All these common-sense observations and many others can be made by any thoughtful general practitioner, internist, surgeon or sociologist. They should dispel the unreasoning fear that state facilities will be swamped by a rising tide of useless and helpless old men and women. The sensible application of these principles should help to encourage reasonable specialization and discourage over-compartmentalization in our profession.

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Editorial Comments

SYMPOSIUM ON FATS IN HUMAN NUTRITION

A symposium on fats in human nutrition, sponsored by the Council on Foods and Nutrition of the American Medical Association, was held at the Tulane University School of Medicine on March 15, 1957. The six papers concerned have recently been published in the *Journal of the American Medical Association*.[1, 4, 5-8]

In reading these papers one is fascinated by the gaps in our knowledge, by our dependence upon animal experimentation, by the limitations of scientific method itself, and by the very real problem of imparting limited and undigested scientific news to the public. The comment below includes reference to two additional publications by other workers.

Average edible fats yield about 9 calories per gram, and when energy demands are high they are a preferred food.[6] They act as vehicles for the fat-soluble vitamins, A, D, E and K, and substances intimately associated with fats provide many flavours. Fats delay emptying of the stomach, acting by means of an inhibitory hormone, enterogastrone. The hunger-dispelling properties of fats are used in certain reducing diets, but whether a high or low fat reducing diet works best has not been settled. Whether the traditional "carbohydrate" obese pasty infant is more susceptible to infection by virtue of the low fat in his diet, or whether fat plays any important part in the immune process, is not clear.

There is a temporary body water loss on a high-fat diet, but in three or four days a new equilibrium is established. There is some evidence that carbohydrate is the food of choice for the castaway because of an economy of water and extracellular electrolyte resulting from glucose administration. In one child observed by Holt,[6] eczema and asthma appeared regularly when fat was removed from the diet and disappeared when it was restored. He suggests that the effect was due to the dehydrating effect of the high-fat, low-carbohydrate diet. Increasing the fat also increased the amount of polyunsaturated fatty acids, essential for various animals. Human experiments hitherto reported on the need for "essential" fatty acids are suggestive, not conclusive.

Holt[6] finds no particular evidence that a generally high intake of fat leads to nausea and vomiting. Excesses of other foods will also do this.

Frederickson[4] gives an admirable summary of the present complicated picture of lipid and lipoprotein metabolism. To add to the difficulties inherent in the problem there is a certain confusion in terminology due to the use of different investigative techniques.

The process by which the newly absorbed fat is removed from the blood is now partially understood. Hydrolysis of triglycerides, catalyzed by the enzyme lipoprotein lipase, is probably an integral part of the process. Heparin, which causes lipoprotein lipase activity to appear in the blood, may form part of the enzyme complex.

The evidence that patients surviving a myocardial infarction have elevated levels of lower density lipoproteins, especially of the Sf 12-400 classes, as first proposed by Gofman, is important. The relative value of the serum cholesterol as compared with the lipoprotein measurements, or atherogenic index, in predicting the likelihood of development of clinical manifestations of atherosclerosis is still controversial according to Frederickson. The recently reported Framingham study (Dawber[2]) indicates that the risk of subsequent myocardial infarction amongst men with high serum cholesterol values is about six times that amongst men with low cholesterol values, in the absence of hypertension or obesity. This important study is concerned with the continuous measurement of cardiovascular disease in a population aged 30-59 since January 1, 1950. From a similar type of study on New York State civil servants (Doyle *et al.*[3]) a similar conclusion is reached.

As W. Stanley Hartroft (previously from the University of Toronto) and W. A. Thomas[5] point out, it is still impossible to state with certainty whether atheroma is primarily a systemic disorder or one of multiple local origin. The most popular current hypothesis is probably that which regards atheroma as a local manifestation in the arterial wall of a general disturbance of lipid metabolism or transport, or both.

These workers, and also C. F. Wilgram, working in the laboratory of Dr. C. H. Best, have reported the production of myocardial infarction in rats by dietary means. This is a striking advance in experimental pathology, as it has hitherto been difficult or impossible to produce this condition in experimental animals. The diets contained high levels of saturated fats such as 40% butter, lard or hydrogenated fat, supplemented with cholesterol, cholic acid, and thiouracil in order to elevate the animals' serum cholesterol levels. Further work on these lines is in progress.

As Ahrens[1] and associates also note, there is a serious lack of direct evidence that atherosclerosis is due to alterations in fat metabolism. These workers feel that the views of Keys and associates on the relationship between total dietary fat, serum cholesterol levels and the incidence of arteriosclerotic heart disease may be too definite. They feel that unproved hypotheses are being proclaimed as facts and that some other factors may be crucial such as, for instance, pyridoxine deficiency, a trace metal, or a bulk former in the diet, which might influence intestinal micro-organisms and in turn the excretion of fats and sterols.

In their experimental work on human subjects these investigators have shown that high

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serum cholesterol and phospholipid values are associated with the ingestion of butter and cocoanut oil as sole dietary fats, and intermediate levels with palm oil, lard, cocoa butter and olive oil. The lowest levels follow the feeding of peanut, cottonseed, corn and safflower oils. Statistical analysis shows that results are best correlated with the mean degree of saturation of fat, as measured by its iodine value. On the other hand, hydrogenation of the highly unsaturated fats vitiates the effect of these fats in lowering the cholesterol level.

In the view of Ancel Keys,[7] most American middle-aged men have hypercholesterolæmia in terms of the world situation; they also have severe coronary atherosclerosis. Keys discusses Eskimo diets and rightly states that we know very little about atherosclerosis in Eskimos, of whom there are not more than about 11,000 in the Canadian Arctic. Even their primitive diet, which contained much fat, was very high in protein and a high proportion of the fat, mostly unsaturated, was derived from fish and marine animals. The Eskimo situation does not contribute anything to the "diet fat-coronary heart disease" hypothesis, nor does that of the Navaho, who get considerably less meat fat, or butterfat, than the U. S. average.

High protein diets may be involved in atherosclerosis, but in man isocaloric variations in protein (casein) had no influence on serum cholesterol, while changes in fat (butterfat or beef tallow) had the usual effect in increasing the levels. In Japan and Italy, with low rates of myocardial infarction, the percentages of calories provided by proteins are almost identical with the values in the United States and Finland with a high incidence of coronary disease.

In 1956 Keys, Paul Dudley White, and B. Brontë-Stewart visited Japan, and they found angina pectoris and myocardial infarction to be uncommon. In Hawaii, Japanese have more atherosclerosis, while in California coronary heart disease is their leading cause of death, as amongst the white population. These rates are proportionate to the average beta-lipoprotein cholesterol concentrations—Shime 124.8, Hawaii 178.2 and Los Angeles 206.0 mg. per 100 ml. respectively.

In Finland, myocardial infarction is extremely common. In Helsinki, the average serum cholesterol concentration in men aged 40-49, members of the Helsinki fire department and of the Helsinki Rotary Club, was over 260 mg. per 100 ml., higher than any other population studied in world-wide researches. Furthermore, in Finland, there is at least one predominantly rural population living at a high rate of energy expenditure and with a very high incidence of coronary heart disease; the amount of fat in the Finnish diet is high and the per capita consumption of butterfat is one of the highest in the world.

Another important clinical point discussed by Keys is the strong relationship between post-surgical, postpartum, and post-traumatic thromboembolic complications and a high fat diet. These complications are very rare in southeast Asia and high in northern Europe and North America.

From a great deal of work on men under controlled conditions, Keys[7] has shown that 1 gram of butterfat has about three times as much effect in increasing serum cholesterol as 1 gram of corn oil or sunflower seed oil has in lowering it. Exclusion of butterfat and meat fats has the greatest effect and this effect may be enhanced by the substitution of such oils as corn oil, cottonseed oil and other plant oils. With a judicious choice of fats in the diet, serum cholesterol level can be controlled without imposing extremely low fat diets.

Both Ahrens[1] and Stare and associates feel that a general prophylactic or therapeutic attack on high fat diets is not justified at present. They do, however, suggest diet therapy for patients with a family or personal history of atherosclerosis. Ahrens[1] and associates have found two regimens effective in lowering serum lipids in out-patients. The first is total vegetarianism in which all dairy products are omitted, except for skim milk, washed cottage cheese, skim milk cheese and egg whites. This regimen has been no less effective, in terms of serum lipids, when supplemented with fish or shellfish once or twice daily. Soybeans, olives, nuts and avocados can be used to advantage. The second regimen consists of a very low fat diet (less than 25 grams per day) supplemented by an ounce or more of corn oil at least three times daily. The basic diet offers modest portions of lean meats, chicken and fish each day. Many of their patients[1] with coronary thromboses have shown improvement on the regimen. Skin xanthomas have disappeared in patients with hypercholesterolæmia or hyperlipæmia.

Stare[8] and associates show that there is no point in reducing cholesterol in the diet, because this does not affect serum levels, which are influenced by the ratio of saturated to unsaturated fats in the diet. The "normal" level for serum cholesterol is difficult to determine. Average readings for North Americans are not necessarily normal in the sense of healthy; perhaps the Japanese level is the most desirable.

While naturally cautious, the general tone of the symposium is hopeful about the treatment and possibly the prevention of atherosclerosis and myocardial infarction. A dietary change in the direction of less total fat, more unsaturated plant fats, and more fish, cereals, grains, vegetables and fruits can do nothing but good to the individual and the community.

HARDING LERICHE

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HYPERTENSION DUE TO UNILATERAL RENAL DISEASE

A recent report by Connor and his associates[1] in the *Bulletin of the Johns Hopkins Hospital* has drawn attention to newer methods in the diagnosis of potentially curable cases of renal hypertension. Clinicians have been searching for such cases since Goldblatt reported the production of hypertension in the dog by constriction of the renal arteries some twenty-odd years ago. Since then patients with unilateral renal disease of widely different sorts have been subjected to nephrectomy in the hope of curing hypertension, with occasional success, but the results were so often disappointing that interest in the field tended to wane and in some centres the search for unilateral renal disease in hypertensive patients almost fell into disfavour.

In the past few years, there has been renewed interest in this subject. It is now apparent that hypertension due to unilateral renal disease is not an extremely rare condition. Furthermore, recent experience indicates that when hypertension is associated with a unilateral lesion which interferes with the arterial blood supply to the kidney the chance of its alleviation by nephrectomy is good. Hence better case selection should improve results and has in fact done so in the group of cases described in this report.

The recognition of cases suitable for nephrectomy may be difficult. Reduction in the arterial blood supply to a kidney often produces changes detectable by intravenous pyelography, such as decrease in size or complete non-function of the kidney. In other patients, the intravenous pyelogram may be perfectly normal. In the latter group of cases, urinalysis and simple tests of renal function are usually of little value in assessing the problem; further investigation is clearly necessary in these cases before the possibility of renal hypertension can be dismissed. Abdominal aortography has been of great value in demonstrating narrowing or obstruction of the renal arteries. Unfortunately, this procedure is unsuitable for the routine screening of patients suspected of having renal hypertension, since it is not without danger and should be performed only by those skilled in the technique. Work done a few years ago at the Johns Hopkins Hospital[2] has led to the development of a differential renal function test which can be more safely used as a routine investigative measure. In patients with hypertension secondary to unilateral renal vascular disease, it was found that there was a marked fall in the volume and sodium concentration of the urine from the involved kidney as compared with urine collected simultaneously from the opposite normal kidney. Subsequent experience with this test, at both the Johns Hopkins Hospital[1] and the Toronto General Hospital,[3] has demonstrated its value in detecting unilateral renal vascular disease when the intravenous pyelogram is perfectly normal. Results also indicate that these studies may be of value in predicting which patients with unilateral renal disease will benefit from nephrectomy. In both centres the test is now done routinely in patients with suspected renal hypertension. If results indicate equal function of the two kidneys, no further investigation is carried out. However, if results indicate renal vascular disease, aortography may be indicated. The paper by Connor *et al.*[1] discussed the care required in the performance and interpretation of these studies which, of course, require cystoscopy and catheterization of the ureters.

Recently the case of a 15-year-old boy with hypertension due to bilateral stenosis of the renal arteries has been described by Poutasse.[4] In this case the hypertension has been relieved by surgical repair of the renal arteries using arterial homografts. Although Connor[1] has suggested that ureteral catheterization studies might be of no value in detecting these cases, recent experience at the Toronto General Hospital[5] indicates that this is at least not always so. The patient in question was a hypertensive young woman with strictures of both renal arteries. Abnormality of the renal vasculature was first suspected because of marked discrepancies in the volume and sodium concentration of urine obtained simultaneously from the two kidneys, and was subsequently demonstrated by aortography. In this case it was possible to excise the arterial strictures and reanastomose the distal ends of both renal arteries to the aorta, with subsequent fall of the blood pressure to normal. This experience suggests the advisability of arteriography in all patients having abnormal functional tests, rather than removing the kidney which is excreting less urine of lower sodium concentration and assuming that the opposite one is normal. Aortography might also disclose unilateral arterial lesions amenable to repair by vascular surgery without recourse to nephrectomy.

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CANADIAN MEDICAL RETIREMENT SAVINGS PLAN

When comparing C.M.R.S.P. rates with those of any other plan, it is important that all features be on the same basis. We have compared the rates of many individual contracts and we found that in no case do the other companies come close to C.M.R.S.P. This is due to the fact that C.M.R.S.P. is a group plan and, as such, benefits from group economies.

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In order to compare tables I and II of the C.M.R.S.P. booklet, you should obtain the *monthly* annuity guaranteed for 10 years, purchased by a *monthly* premium of $100.00, under which the death benefit before retirement is the return of premiums with 3% interest plus accumulated dividends. If the individual contract is participating, both the guaranteed and the estimated benefits should be compared. If the contract is non-participating it is quite difficult to compare it with C.M.R.S.P., but any comparison should take into account the fact that guaranteed benefits under the C.M.R.S.P. contract are minimum benefits and should be substantially increased by dividends.

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Some trust companies are offering individual pooled common stock funds under which the expense charge is ¾% of the total fund, each year. Most mutual funds have an investment charge of ½% of the total fund, each year, plus acquisition or sales cost of 6 to 9% of contributions made. C.M.R.S.P.'s total expense charge is ½% of the value of the fund, each year. There is no acquisition or sales cost. C.M.R.S.P., like other funds, re-invests dividends without charge. This reduced expense rate could make an appreciable difference in the accumulated value of your savings at retirement.

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C.M.R.S.P. brings to you the lowest expense factors available and the manpower resources of Canada's largest financial institution. In addition C.M.R.S.P. guarantees now, annuity rates applicable to a portion of each member's common stock accumulation, whereas individual trust and mutual funds must purchase annuities at market price at the time of your retirement. This is an important factor in view of the trend to improvement in mortality.

When comparing the offerings of other plans with C.M.R.S.P., you should determine the answers to these questions:

1. Does the plan provide a more advantageous interest rate which is guaranteed for your lifetime?
2. Does this interest rate apply to all future contributions as well as to those made in the current year or in the next three or five years?
3. Does the plan guarantee annuity rates which will be used at your retirement to translate your savings into retirement annuities?
4. Does the plan provide for a return of all contributions plus a realistic interest rate if death occurs prior to retirement?
5. Does the plan provide you with the option of varying the amount of your savings, year by year?

Compare the answers which you receive with the information set out in the C.M.R.S.P. brochure. Acting in your interest, the C.M.A. plan was devised to provide the best long-term guarantees available. The level of these guarantees is designed to assure reasonable earnings coupled with safety and satisfactory annuity rates.

All members are again reminded that to obtain tax-deferment on contributions relative to 1957 income, it is necessary that they be enrolled in a registered retirement savings plan before December 31, 1957. The prompt return of your application for enrolment in C.M.R.S.P. will protect your position in respect of deposits made before February 9, 1958.

Medical News in brief

DEATHS IN U.K. TEACHING AND NON-TEACHING HOSPITALS

An investigation of mortality in the teaching and non-teaching hospitals of Britain by a Medical Research Council team has disclosed some surprising figures (*Lancet*, 2: 785, 1957). The investigators studied mortality rates from appendicitis, perforated peptic ulcer and hyperplasia of the prostate, and the statistics apply to the years 1951, 1953 and 1954. During these three years the case fatality rate from appendicitis with peritonitis was 3.3% in teaching hospitals, and 6.6% in non-teaching hospitals. For perforated peptic ulcer the mortality figures during these years were 7.2% in teaching and 9.7% in non-teaching hospitals; comparable figures for prostatic hyperplasia were 4.1% and 7.6% respectively. Comparable differences between the two classes of hospital in Britain were found in deaths from diabetic coma. In the case of prostatic disease, there may well be differences in selection of patients for operation, and it is generally agreed that patients admitted to non-teaching hospitals for prostatectomy are on the whole in poorer physical condition. It is however hard to explain the differences in the case of appendicitis. Further clinical and epidemiological studies are needed to elucidate the situation.

PROMETHAZINE IN CLINICAL ANÆSTHESIA

In a California centre, Watrous and his colleagues (*Anesth. & Analg.*, 36: 38, 1957) used promethazine (Phenergan) either intramuscularly or intravenously in approximately 400 cases as preoperative premedication. Used on the night before operation, it is a useful sedative in oral dosage of 25-50 mg. or as a hypodermic injection with 100-200 mg. of pentobarbital orally. For preoperative sedation, it may be given intramuscularly in a dose of 25-50 mg. two to three hours before operation, followed by 50-100 mg. of meperidine and 0.3-0.4 mg. of atropine or scopolamine one hour before operation starts. In 337 patients promethazine was given intravenously for induction of anæsthesia before intravenous thiopental, or gas and oxygen, to calm apprehensive or disturbed patients, to give sedation before conduction anæsthesia, to supplement anæsthesia, to protect against bronchospasm, or to protect against shock. Dosage was mostly 25-50 mg. This supplement of promethazine reduced considerably the need for supplementary doses of barbiturate and gave a smooth anæsthesia with less respiratory depression. It was well tolerated by poor-risk patients and helpful in anæsthetizing asthmatics.

NATURAL HISTORY OF LUNG CANCER

Karnofsky and his colleagues from New York (*Radiology*, 69: 477, 1957) have made an intensive study of the natural history of lung cancer in a series of 80 patients coming to autopsy. They suggest a classification of lung cancer based on the clinical pattern and not the histology. They recognize the following variations:

Type 1. Clinically localized.—This type tends to grow and extend within the lungs with no evidence of metastases until terminal stages. These are the candidates for surgery, though this type of cancer may grow rapidly. Out of the 80 cases studied, 30 were classified in this group.

Type 2. Clinically early generalized dissemination.—In this type distant metastases often occurred before or simultaneously with pulmonary symptoms. Growth is rapid in all parts of the body from the time of clinical onset, and survival time after clinical onset may be less than six months. There were 28 cases in this group.

Type 3. Organ-specific distant metastases.—These are subsidiary types of metastases in which the cancer seems to grow particularly well in certain distant organs. These secondary lesions occur early and may represent the initial complaint. Principal variants are (a) cerebral type; (b) bone type; (c) hepatic type. Of these three variants, there were ten, seven and five cases respectively.

KNOCK-KNEE IN CHILDREN

To learn more of the natural history of knock-knee, Morley of the Institute of Orthopædics, London, England, (*Brit. M. J.*, 2: 976, 1957) made over 1000 examinations on unselected normal children from infant welfare clinics and a school. He found that the incidence of knock-knee increases until three to three and a half years of age and then declines. Between three and three and a half years of age only 26% of children had less than one inch of knock-knee, 52% had between one and two inches and 22% had a knock-knee of two inches or more. There was no sex difference in the incidence of knock-knee; at five years and over only 1-2% of children had a knock-knee of two inches or more. Knock-knee tended to be associated with overweight, but not with valgus feet, flatfoot, illness, vitamin supplementation, breast feeding, and the age of beginning walking. The knock-knee found in toddlers usually improves without treatment; apart from operative procedures, no effective treatment for it is known. Morley thinks that knock-knee in children under seven can probably be safely ignored unless excessive or associated with some cause such as epiphyseal damage.

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GENERAL PRACTICE

SURGICAL TRAINING

THE EXECUTIVE of the College of General Practice of Canada forwarded the following letter to the Canadian Medical Association and copies of it to l'Association des Médecins de Langue Française du Canada and The Royal College of Physicians and Surgeons of Canada:

October 31, 1957

Dr. A. D. Kelly,
General Secretary,
Canadian Medical Association,
150 St. George Street,
Toronto 5, Ontario.

Dear Doctor Kelly:

I am directed by the Executive of the College of General Practice of Canada to call your attention to the resolution recently passed by the Council of the Royal College of Physicians and Surgeons of Canada regarding surgical teaching in the Royal Jubilee Hospital, Victoria, in particular, and surgery done by the general practitioner in general. We understand that this resolution has been circulated directly by the College to various hospitals throughout Canada.

While giving due respect to their opinions we believe this action by the Royal College to be unfortunate. Surely this matter should have been brought before the Canadian Medical Association before such action was taken. The College of General Practice of Canada is opposed to all divisive influences in Canadian medicine. We recognize the role of the Canadian Medical Association and l'Association des Médecins de Langue Française du Canada as the two national bodies governing all the internal workings for the welfare of our profession.

We wonder if their opinion expressed with respect to the specialty of surgery applies equally to the other specialties, which demand equally long and arduous training. Principles governing one specialty should be applicable to all.

We believe that the Royal College of Physicians and Surgeons is doing a great and necessary work in the training and accreditation of specialists. Our hope is that this work will continue to expand so that more of these well-trained men will seek a place in our smaller towns where a useful career awaits them. We agree with the paramount place given to the patient's welfare, and the College of General Practice shares the ideal of adequate training expressed by the Royal College of Physicians and Surgeons. These ideals give a common origin to both Colleges. But we feel that the stand taken by the Royal College of Physicians and Surgeons as expressed in their resolution is unrealistic in confronting medical service needs of Canada as a whole today.

Moreover, the stand taken by the Royal College is not consistent. There are quite a number of competent general surgeons in Canada restricting their work to that specialty who have not had the training demanded by the resolution and yet have been certified by the Royal College and in many cases have been awarded its highest degree. There are many more doing general practice yet certified by the Royal College in surgery without either the required training or examination. We do not point out these things as being in error but as showing the inconsistency of the resolution in question.

The fact is that much of the work which the resolution claims should be done by the specialist, must indeed be done by the general practitioner in our present situation. This contention can be supported by information from many sources.

We of the College of General Practice therefore welcome all such teaching projects as set forth in Dr. Anderson's article in the December 15, 1956 issue of *The Canadian Medical Association Journal.*

We are forwarding a copy of this letter to the Royal College of Physicians and Surgeons of Canada and to l'Association des Médecins de Langue Française du Canada.

Yours sincerely,
(signed) W. V. JOHNSTON, M.D.,
Executive Director.

UPJOHN SCHOLARSHIPS FOR POSTGRADUATE EDUCATION

THE EXECUTIVE of the College of General Practice of Canada has accepted the generous offer of twelve $500 scholarships or awards annually from the Upjohn Company of Canada. The awards will go to two general practitioners from Ontario; two from Quebec (one French-speaking and one English-speaking), and one from each of the other provinces, to help these doctors defray expenses while attending a postgraduate course.

Each Provincial Chapter is required to set up a Provincial Award Committee, subject to the approval of the College, and it will be the responsibility of each Provincial Award Committee to choose the recipient or recipients in its own province. The Executive of the College has asked each Provincial Chapter to establish its Award Committee promptly, as these scholarships are available beginning January 1, 1958.

The Executive also states that applications may be submitted at once to the secretaries of the Provincial Chapters of the College. It is hoped that Provincial Award Committees will receive applications and review them so that awards may be made early in the new year.

Recipients must be active or associate members of the College of General Practice of Canada.

The award winners will submit their choice of courses to the Award Committee for their approval. The course must be of at least two weeks' duration. It can be in any place in Canada or the United States and it may be an organized established course or a specially arranged course of instruction at a hospital or teaching centre.

Within a month of completion of the course the recipient will submit to the Executive Director of the College of General Practice of Canada a signed record of his attendance and a written report of the course's value. These courses will qualify for formal postgraduate study credits.

NEPHRITIS RESEARCH

THE COLLEGE of General Practice proposes to collaborate with the Research Institute of the Hospital for Sick Children and the Department of Medicine of the Toronto Western Hospital in a one-year study of the relation of streptococci to acute nephritis in the Metropolitan Toronto Area. The Research Committee of the College of General Practice is requesting that information and patient material be referred from all the general practitioners in the area to the study group.

Research Fellows have been appointed at each hospital and the work is being done in collaboration with the Division of Laboratories of the Ontario Department of Health. The project offers certain free investigative services, but is not intended to interfere with the management of the patients in any way. The purpose of the work is to: (1) Define the incidence of streptococcal infection in acute nephritis. (2) Observe the variability of kidney involvement in relation to the infection. (3) Collect streptococci and sera associated with kidney disease for further studies in the pathogenesis of nephritis.

It will be necessary to culture the throats and collect the blood for streptococcal antibody studies in all patients seen. It is proposed that each individual referred to hospital have: (1) Throat culture on admission. (2) Ten c.c. of clotted blood on admission for antibody studies. (3) Ten c.c. of clotted blood two weeks later or on discharge from hospital if sooner, for further antibody studies.

In order to provide as good sampling as possible, it is proposed that practitioners in Metropolitan Toronto permit these studies to be carried out on their patients with acute nephritis so far as is possible. Two alternatives are possible for the management of the patient:

1. *If the physician wishes the patient admitted to hospital for therapy,* the patient is referred directly to the staff physician preferred by the family doctor, or if no staff physician is defined, the patient is admitted in the usual manner.

2. *If the family doctor prefers to treat the patient at home,* it is desirable that the patient be referred immediately to the Emergency Department of either hospital for the collection of specimens by the Research Fellows (for children under 15 years, Hospital for Sick Children; older patients, Toronto Western Hospital). After this the patient returns home immediately. If it is not feasible to send the patient to the hospital, arrangements can be made for a home visit by the Research Fellow, on request, to collect the specimens.

There will be no charge whatsoever associated with the research.

Since this is the first time that the general practitioners have been invited to participate in a research problem of this nature under the ægis of the College of General Practice, it is hoped that all will co-operate fully to make this a successful study.

Research Fellows: Hospital for Sick Children: Dr. Paul Azzopardi, EM. 6-7242; Toronto Western Hospital: Dr. W. Bladek, EM. 8-2581.

G. ALLAN PENGELLY, M.D.,
Chairman of Research Committee,
Toronto Branch,
College of General Practice.

POSTGRADUATE COURSES FOR GENERAL PHYSICIANS

CANADA

Second Scientific Convention, College of General Practice of Canada, Royal Alexandra Hotel, Winnipeg, Manitoba, April 14-16, 1958.

ONTARIO

Refresher Course in Public Health and Preventive Medicine, School of Hygiene, University of Toronto, February 10-12, 1958. Fees: Three days $35; February 12 only, $15.

Section of General Practice Clinic Day, Hamilton, April 16, 1958.

Fracture Course, Niagara Falls Medical Group, May 7-9, 1958.

Review Lectures in Medicine, Women's College Hospital, Toronto; first and last Monday evenings of each month, September to June.

QUEBEC

General Practitioner Course, Montreal General Hospital (Dr. William Storrar, Registrar), March 17-22, 1958.

U.S.A.

National Assembly, American Academy of General Practice, Dallas, Texas, March 24-27, 1958.

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Association Notes

EXECUTIVE COMMITTEE MEETING

The Executive Committee of the Canadian Medical Association held its fall meeting at C.M.A. House, Toronto, on November 1, 2 and 3, 1957, under the chairmanship of Dr. Norman H. Gosse. This was a busy weekend because not only were the regular meetings of the Executive Committee held on Friday and Sunday, but a special conference was held with the commissioners of Trans-Canada Medical Plans on Saturday, at the Park Plaza Hotel. Furthermore, on Monday, November 4, the Advisory Committee of the Executive to the Federal Government went to Ottawa to discuss with the Honourable J. Waldo Monteith, Minister of National Health and Welfare, certain problems of mutual interest.

D.V.A.—The Committee learned that the Treasury Board had stated that they were prepared to apply a D.V.A. fee schedule of 90% of provincial fee schedules. This would replace the uniform schedule across Canada hitherto applied. It would be applied on the understanding that provincial medical bodies would freeze their fee schedules for a period of three years after the application of the new rates. The Executive Committee, however, did not feel that they could wholeheartedly recommend acceptance of this 90% schedule, and the Advisory Committee to the Federal Government was instructed once more to discuss the possibility of a 100% settlement with the Minister of Veterans Affairs. It was agreed that the result of the Advisory Committee's negotiations would be the subject of a mail ballot.

Canadian Medical Retirement Savings Plan.—The Committee was informed of the present status of the Canadian Medical Retirement Savings Plan; 400 participants have been enrolled, the largest number coming from Ontario (131) and British Columbia (90). It was interesting to note that 22 applicants wished to participate only in the insured plan, and 77 only in the common stock plan; of the remainder 131 had indicated a 50-50 proportion.

It was again emphasized that each member of the Association must be aware that **unless his application card to participate in the Savings Plan was received at C.M.A. House before December 31, he would be unable to claim exemption of his contributions for the taxation year 1957.** The booklet describing the Medical Retirement Savings Plan is at present being translated into the French language and will soon be available. It was emphasized that membership in either the Canadian Medical Association or l'Association des Médecins de Langue Française du Canada would suffice for entry into the Plan. A trusteeship committee is to be set up, with corresponding members in the divisions of the C.M.A.

Hospital accreditation.—The Executive Committee agreed with a draft notice of withdrawal to be transmitted by the Canadian Medical Association to the Joint Commission on Accreditation of Hospitals, serving notice of withdrawal from the latter body on December 31, 1958. This means that an all-Canadian program of accreditation will be inaugurated on January 1, 1959. The Canadian Commission is proceeding towards incorporation and has appointed Dr. W. I. Taylor as full-time director as of last September.

Advisory Committee to the Federal Government.—It was agreed that at the meeting on November 4, the Advisory Committee would discuss with the Minister of National Health and Welfare such subjects as liaison between the medical profession and the Government, Bill 320, Indian affairs, representation of the C.M.A. on the Canadian delegation to the World Assembly, and the current status of the DAMDSAB. It was also agreed that this Committee would indicate to Government its support of a request by the Association of Canadian Medical Colleges that funds for medical research be increased. It was agreed that amounts at present available for research in Canada are totally inadequate to meet the many applications.

Salaries and qualifications of public health personnel.—The Executive Committee studied the third revision of the report on salaries and qualifications of public health personnel, which indicates qualification requirements and minimum salaries for public health personnel in Canada. It endorsed this schedule, and agreed that any advertisements for public health personnel which did not meet this minimum schedule would be refused space in the *Canadian Medical Association Journal.*

Annual meeting finances.—The committee appointed to study annual meeting finances made recommendations to the Executive Committee, which were accepted. It was suggested that entertainment at the annual meeting should remain the responsibility of the host division, but that all other revenues should be collected and expenses met by the Canadian Medical Association, and any balance divided equally between the host division and the Canadian Medical Association.

C.M.A. staff.—The Executive Committee has approved the appointment of Mr. B. E. Freamo as Assistant Secretary (Economics); Mr. Freamo's services had been made available to the Canadian Medical Association with the concurrence of the Ontario Medical Association, for which body Mr. Freamo previously worked in a similar capacity. The Committee also heard with regret the resignation of Mr. L. W. Holmes, Assistant Secretary (Public Relations), to take effect on December 1, 1957.

Canadian Medical Traffic Accident Research Foundation.—Progress was reported with the establishment of this Foundation. The charter is likely to be signed within a month or so and the Ford Motor Company of Canada Ltd. has already made available $5000 for a pilot study, to be undertaken by Dr. Ruth McDougall of Montreal.

Divisional meetings.—The President of the C.M.A., Dr. Morley Young, reported on his visits to eight divisional meetings, commenting that it would serve a useful purpose if the president and secretary of each division made a habit of visiting some other division at the latter's annual meeting each year. He also stressed the need for closer association between tariff committees and those responsible for prepaid schemes. He detailed the view among many physicians that some effort should also be made to reduce the time element in general medical training. Dr. Young advocated the policy of having one or more speakers from other professions at C.M.A. and divisional meetings, and also of associating the nursing profession more closely with medical meetings.

The Committee heard that Newfoundland wishes to hold its annual meeting in May, and not in September as previously.

World Medical Association.—The report of the C.M.A. delegates to the General Assembly of the World Medical Association in Istanbul, September 29—October 5, 1957, was heard. The delegates, Dr. E. S. Mills of Montreal and Dr. N. H. Gosse of Halifax, had gained the impression that the prestige of the World Medical Association has been much enhanced in recent years. They said: "Except for the impact upon the permanent secretariats at Geneva, the tangible effects that Canada can derive from W.M.A. may well be questioned. Yet the picture of the nations in action in the atmosphere of professional brotherhood that there obtains, the obvious need for help on the part of many nations, and the contribution the West can and does make for that need, leaves no doubt in the minds of your delegates that Canada has an obligation that it should assume." After hearing this report the Executive Committee decided to set up a committee to study the relationship between C.M.A. and W.M.A., with a view to making Canadian membership in this Association more effective. The subcommittee appointed to nominate a president for the World Medical Association in 1959, in which year the W.M.A. Assembly will be held in Montreal, reported; the nomination of Dr. Léon Gérin-Lajoie of Montreal was accepted, with a proviso that if Dr. Gérin-Lajoie could not accept the post Dr. Norman H. Gosse of Halifax should be offered the presidency. Arrangements for the 13th General Assembly in Montreal, September 6-12, 1959, were discussed.

Budget and finance.—The Budget Committee under the chairmanship of the Honorary Treasurer presented a detailed forecast of the financial affairs of the Association for 1958. In predicting a revenue of $605,000, it was noted that the two major sources of income are advertising ($350,000) and membership fees ($204,000). The expenditures reflect the range of activities of the Canadian Medical Association which are constantly increasing. Again, these outlays may be broadly classified into C.M.A. Publications ($378,000) and all other projects which are administered under the generic heading of Secretarial ($260,000). On the basis of available information a deficit in the year's operations of $35,000 was predicted, with the cautionary comment that this figure might be substantially reduced or might be converted into a small surplus. The Executive Committee examined all figures in detail and received explanations of individual items which were not clear.

Ninety-First Annual Meeting, Halifax.—The ninety-first annual meeting of the Canadian Medical Association will be held in Halifax, June 16-20, 1958. The progress report was given by the President-elect, Dr. A. F. VanWart. There will be a coloured television program for two and a half days, by the courtesy of Smith, Kline and French, as at the 1957 meeting. In order to indicate that this meeting concerns all the Atlantic provinces, luncheons will be held on Tuesday, Wednesday, Thursday and Friday with distinguished speakers from Nova Scotia, New Brunswick, Prince Edward Island and Newfoundland, respectively. Many specialist societies will be meeting either in Halifax or in other Maritime cities at or around the time of the annual meeting. It is expected that the Executive Committee of the C.M.A. will meet in Charlottetown, P.E.I., on June 13 and 14 and fly from Charlottetown to Halifax on Saturday evening, June 14, so as to be present at the annual church services in Halifax the next day.

Ninety-Second Annual Meeting, 1959.—The arrangements for the ninety-second annual meeting to be held in Edinburgh, Scotland, July 18-24, 1959, were described to the Executive Committee. The official travel agents, University Tours, report enquiries on behalf of no less than 1400 Canadian persons already planning the trip. It was again urged that all prospective C.M.A. travellers consider their plans *now*, in view of the enormous problems of travel at the height of the tourist season and of housing in Edinburgh. C.M.A. members should list their names with University Tours, 2 College Street, Toronto, where master lists are being maintained. A list of C.M.A. Sectional Officers is 95% complete and the Central Program Committee is about to authorize invitations to Canadian speakers for the scientific program. In 1959 the General Council of the C.M.A. will meet in Toronto at some date in relationship to the annual meeting of the Ontario Medical Association, which will take place May 25-29. Whether or not the Executive Committee will hold a meeting in Edinburgh is as yet unsettled.

C.M.A. Publications.—The Editor reported on progress in the *Canadian Medical Association Journal* and the new publication, the *Canadian Journal of Surgery*, and pointed out some minor changes in the *Canadian Medical Association Journal* including the use of a somewhat larger type for such sections as Provincial News, Obituaries and Book Reviews, the growing policy of reporting as many national and other medical meetings in Canada as possible, and the fact that the Editor had been chosen as a rapporteur for the Second World Conference on Medical Education to be held in Chicago in 1959. He said that the *Canadian Journal of Surgery* had made a promising start, but that the subscription list had by no means reached the

target set. It was essential that those with the welfare of Canadian surgery at heart be induced to subscribe to the Journal and to support it with contributions. The Managing Editor reported that the profit for 1957 was considerably less than that in 1956, and pointed out that although prospects for 1958 appeared bright, various factors such as falling stock market quotations, increased unemployment and world unrest had to be watched and assessed carefully. Advertising budgets were sensitive, reflecting to a considerable degree the balance sheet of business, and therefore caution was needed in the management of the Journal finances.

L'Association des Médecins de Langue Française du Canada.—It was reported that the President-elect, Dr. VanWart, had represented the C.M.A. at the annual meeting of l'Association des Médecins de Langue Française du Canada in Quebec last September. It was also reported that l'Association had nominated the following three representatives on the Liaison Committee with the C.M.A.: Dr. R. L. Duberger of Sherbrooke, Dr. J. M. Laframboise of Ottawa, and Dr. Albert Jutras of Montreal.

Secretaries' Conference.—It was agreed that the invitation of Dr. G. G. Ferguson to the divisional secretaries of the C.M.A. to meet in Vancouver, February 20-22, 1958, should be accepted.

Applications for Affiliation.—The application of the Canadian Hearing Society for affiliation with the C.M.A. was approved for transmission to General Council next June.

C.M.A. House.—It was agreed that the Housing Committee should study a long-range plan for developing the property of C.M.A. House, so as to provide accommodation for future expansion. It is likely that an architect will be engaged to study the site and prepare initial plans for future structure, needed for the growing activities of the Association.

Relative value fee schedules.—It was reported that the committee set up to study relative value fee schedules had met and made certain recommendations for future studies. The report showed that a considerable sum of money would be necessary, first for the activity of a committee on methodology and then for the co-ordination of work by provincial study committees on unit values. The project would take at least three years. It was agreed that such a project was feasible and should be undertaken. As a preliminary, it was recommended that certain basic studies be undertaken by the Secretariat, including possible methods of financing the whole project. It was also agreed that not only relative but also absolute values of fee schedules should be studied, in order to assess the total monetary value of a doctor's work in the community.

Joint Conference of T.C.M.P. Commission and C.M.A. Executive Committee.—As stated above, the commissioners of Trans-Canada Medical Plans and the C.M.A. Executive met together at the Park Plaza Hotel on Saturday, November 2, with Dr. Norman H. Gosse in the chair. The object of the conference was to clarify certain relationships between T.C.M.P., its member plans and the medical profession in carrying on the extension and improvement of non-profit, voluntary prepaid medical care programs providing for the needs of the people of Canada.

National Enrolment.—The first problem studied related to the selling of a national program. A brief was presented by Dr. M. R. MacCharles, chairman of the board of Manitoba Medical Services, suggesting the establishment of a new national T.C.M.P. underwriting organization for over-all national contracts. There was much discussion of the situation in which the minority of T.C.M.P. felt unable to go along with the majority in accepting a national contract. It was finally agreed that in this situation the first step was to seek coverage by a member plan in an adjoining area; if this failed, coverage should be sought by other carriers; if both these steps failed, the contract should be turned down. It was also agreed that this would be an interim measure pending the results of study of the plan proposed by Dr. MacCharles.

Service or indemnity plans.—The question whether T.C.M.P. should continue to develop its objectives solely through service plans or through service and indemnity plans was keenly debated. It was felt that the C.M.A. should go on record as stating that a service plan is the more desirable and more beneficial. It was recommended to provincial divisions without service plans that they develop such programs as a matter of urgency. The present structure of T.C.M.P. in which both service and indemnity plans were represented should continue, but only so long as service plans sponsored or approved by a division were not available in every province of Canada.

Separation of prepaid medical care from prepaid hospital care.—The conference recommended that the C.M.A. encourage the separation of prepaid medical services from prepaid hospital care, because the former is medical business and should be handled by medical persons.

Medical and plan interests.—As a means of establishing general policy guidance, certain areas were defined as areas of joint interest to the medical profession and to the voluntary plans, while others were primarily of medical interest or primarily of plan concern. For example, it was agreed that such items as fee schedules for prepayment use, professional agreements with service plans, the problem of excessive utilization and benefit provisions of service plan contracts were matters of joint concern. It was agreed on the other hand that discipline of members for unethical practices was entirely the responsibility of organized medicine, while such matters as the methods of collecting subscription income and age limitations and general enrolment regulations were primarily a responsibility of member plans.

Improved T.C.M.P.–C.M.A. liaison.—Various methods of improving liaison between T.C.M.P. and the C.M.A. were debated. It was finally agreed that no additional representatives should be nominated to the T.C.M.P. commission, but that joint conferences should be held as required to discuss

mutual problems. It was also recommended that the T.C.M.P. commission would permit the presence of observers from the divisions of the C.M.A., sent at the divisions' expense.

T.C.M.P. and the public.—Finally, the suggestion was accepted that T.C.M.P. should do more to bring before the public the basic value of medical care. It was generally agreed that food, clothing and shelter were primary necessities of life. It was time to emphasize to the public that in a civilized community a first essential was medical care and that this item ought to be budgeted for and assigned as much importance as the other three.

MEDICAL MEETINGS

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF CANADA

The twenty-seventh annual meeting of the Royal College of Physicians and Surgeons of Canada was held at the Sheraton-Mount Royal Hotel, Montreal, on Friday and Saturday, October 18 and 19, 1957. At the business meeting on Friday afternoon, Dr. John W. Scott, Dean of Medicine in the University of Alberta, was elected president; the vice-president in medicine is Dr. Francis S. Brien of London, Ontario, and the vice-president in surgery is Dr. Louis-Phillipe Roy of Quebec City. The immediate past president is Dr. R. M. Janes of Toronto, the honorary treasurer, Dr. K. T. MacFarlane of Montreal, the secretary, Dr. James H. Graham of Ottawa and the honorary assistant secretary, Dr. W. Gordon Beattie of Ottawa.

Division of Medicine

At the session on Friday morning, in a paper on diffuse interstitial fibrosis of the lung, Dr. D. V. Bates of Montreal stressed that the diffuse capacity of the lungs for oxygen and carbon dioxide (DCO) was affected early in this rare disease, as contrasted with other types of pulmonary fibrosis. Finger clubbing occurs early and other symptoms and signs are noted while fine fibrosis is only faintly seen in the radiograph. Dr. R. M. Cherniack of Winnipeg described the modern management of respiratory acidosis and made the interesting observation that it is in part due to metabolite overproduction by the overworking respiratory muscles. Dr. Charles Lépine and co-workers of Montreal described their cardiopulmonary studies in kyphoscoliosis and indicated that in most cases this is a form of chronic cor pulmonale. Dr. Joseph Dvorkin of Edmonton described the medical aspects of open-heart surgery with the pump-oxygenator and noted the occurrence of convulsions, acidosis, cardiac arrhythmias and gastric dilatation. Dr. C. E. van Rooyen of Halifax described an epidemic of infant bronchiolitis occurring in Nova Scotia in 1956, and noted that members of the adenovirus group had been isolated. Drs. N. M. Lefcoe and G. W. Manning of London, Ont., described their phonocardiographic studies in mitral stenosis and indicated that while the Q-M_1 and the 2-0.5 values are of some interest they cannot be used to elucidate degrees of mitral stenosis. The 1957 Medallist in Medicine of the Royal College of Physicians and Surgeons, Dr. R. D. Rowe of Toronto, correlated the clinical, hæmodynamic and known anatomical changes that occur in the pulmonary circulation of the newborn, in a brilliantly conceived and beautifully presented study.

Dr. K. W. G. Brown of Toronto described the studies of his group with various drugs in intermittent claudication. The rigid application of the double-blind technique resulted in the finding that there is no effective drug, and where disability is severe, surgery is required. Dr. R. L. MacMillan of Toronto discussed the management of 30 patients on prolonged out-patient anticoagulant therapy, and concluded that it is feasible where the need is great and adequate control facilities are available. Dr. J. S. Crawford of Toronto described his experience in the development of a department of physical and rehabilitation medicine at the Toronto Western Hospital.

At the session on Friday afternoon, Drs. J. R. Anderson of New York and D. R. Wilson of Edmonton showed that in diabetes during ACTH administration there was a significantly higher excretion of 17-ketosteroids and 17-hydroxycorticosteroids than in normal subjects and discussed the significance of this finding. Drs. J. C. Beck and W. Leith of Montreal presented data indicating that a combination of 9-alpha-fluorohydrocortisone and hydrocortisone produced less undesirable side effects than the former alone in adrenal insufficiency. Drs. C. Ezrin and P. J. Moloney of Toronto demonstrated beautifully the developing of insulin-neutralizing antibodies in the human body, irrespective of the species of animal providing the insulin. They made the point that such antibodies "destroy" extracted insulin and that the diabetes is *not* due to such neutralization of the patient's own insulin.

Dr. D. L. Wilson and his co-workers of Kingston demonstrated that I^{131} can cause thyroid malignancy in the rat, preventable by the administration of thyroid extract. It was conceded, however, that this probably does not occur in man. Dr. Louis Horlick of Saskatoon presented his own work suggesting that polyunsaturated fatty acids have no consistent or specific depressant effect on the serum cholesterol. Dr. R. P. Howard, formerly of Montreal and now of Oklahoma City, pointed out that lower-density lipoproteins (Gofman S_f 12-2- and 20-100) were unaffected or inconsistently affected by gonadal steroid administration.

Dr. R. D. Drysdale of Halifax demonstrated that in chronic leukæmia there is a tendency to increased iron turnover while in acute leukæmia there is decreased turnover. Drs. J. L. Hutchison, S. R. Townsend and D. G. Cameron of Montreal suggested that cobalt^{58} tagged vitamin B_{12} may be a safer and more valuable agent for hæmatologic study than its cobalt^{60} tagged analogue. Drs. I. T. Beck, R. D. MacKenna and J. C. Beck of Montreal produced evidence casting doubt on the validity of utilizing uropepsin and blood pepsin levels as a guide to gastric secretion. Dr. D. J. MacIntosh and his co-workers of Montreal suggested that the oxygen ventilatory equivalent in mitral stenosis parallels the severity of the obstruction and recommended the use of this parameter as a guide in selecting patients for mitral commissurotomy.

Division of Medicine

At the session on Saturday morning, Dr. Allen Gold of Montreal produced case histories and other evidence to show that iodine was a double-edged sword in thyroid disease. Excessive iodine intake may lead to

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(1) development of goitre in a patient with a normal thyroid gland; (2) rapid increase in size of an existing non-toxic goitre; (3) development of hyperthyroidism in a previously non-toxic goitre. Use of iodine may make diagnosis difficult, and a therapeutic trial of the drug in suspected "borderline" hyperthyroidism is no longer justified. Dr. J. H. Darragh and colleagues of Montreal described their results in treatment of diabetic patients with tolbutamide. They had worked with the drug for one year and considered it useful. There is very little acute toxicity (one case of papular rash). Hypoglycæmia was seen only when tolbutamide and insulin were given together. Selection of patients could still only be on an empirical basis.

Dr. T. B. Rasmussen of Montreal described his experience in 12 cases of hypophysectomy for advanced breast carcinoma. In eight cases temporary remission had occurred. Paresis and urinary difficulty due to secondaries had improved with this treatment. There was no known method of selecting suitable cases, and the operative mortality was 5%. As the result of 2000 determinations of serum protein fractions by paper and by free electrophoresis, in the Tiselius apparatus, Dr. Eleanor McGarry of Montreal declared that free electrophoresis is accurate but expensive and time consuming. Normal values for protein distribution obtained by the paper and boundary methods are in good agreement, but there is considerable disagreement between the results of salt fractionation and electrophoresis. Salt fractionation picks up only about 50% of the protein abnormalities detected by electrophoresis.

Three cases of pure red cell aplasia were described by Dr. Lorne Shapiro of Montreal, in which there was anæmia with aplasia of the erythropoietic cells of the bone marrow, but no involvement of leukopoiesis. The first case was unique in showing a clearcut response to steroid therapy on three occasions. This patient also had a mediastinal tumour, whereas the other two showed evidence of acute hæmolysis. Exogenous hæmochromatosis associated with multiple transfusions of blood over a protracted period in anæmic patients was described by Dr. F. S. Brien of London, Ontario. One patient had received the equivalent of 150 litres of blood or 75 g. iron before developing infections and later heart failure. The other patient developed signs of leukæmia late in his 4½-year illness.

Dr. G. C. Walsh and his co-workers of Vancouver described two cases of that very rare condition known as the Dubin-Johnson syndrome and consisting of an excess of lipochrome-like pigment in the liner cells, with jaundice but without disease. Dr. B. B. Fast of Winnipeg described work suggesting that, in hepatic insufficiency, the coma which frequently occurs, and which he, with others, has noted to be associated with increased blood ammonia levels, may be the result of the action of ammonia-producing intestinal bacteria. Improvement resulted from the exhibition of non-absorbable antibiotics.

Dr. Bram Rose and his co-workers of Montreal described the occurrence of atypical amyloid disease in two sisters, with the suggestion that hyperergic mechanisms may have been responsible. Drs. M. Kaye and G. W. Halpenny, Montreal, described the features of 13 cases of occult chronic pyelonephritis, and indicated that many such patients will be believed to have chronic glomerulonephritis unless very carefully investigated. Dr. A. L. Gordon of Montreal described two patients with a rare familial kidney disease associated with deafness who had been followed to autopsy, and discussed the genetic implications.

DIVISION OF SURGERY

The Friday morning session was devoted to presentations on the surgery of trauma. Dr. Claude Bertrand of Montreal stressed the value of cerebral angiography in investigation of head injury. Out of 215 cases studied by this method during 1948-1956, an accurate diagnosis and localization of the lesion were made possible by cerebral angiography in 108, while 101 patients were not submitted to surgical exploration because of a negative angiogram. Dr. W. R. N. Lindsay of Toronto stated that a long-term follow-up of 150 cases of fracture of the os calcis had disclosed a high proportion of poor results, for only 17% were free of pain after 10 years. The tremendous force needed to fracture an os calcis must lead to extensive trauma to surrounding tissue. Pain in the hindfoot is shown not to be due to subastragaloid arthritis; the latter was discovered radiologically in many cases without subastragaloid pain. On the whole, conservative treatment proved best.

Dr. F. G. Inglis of Montreal brought evidence to support the idea that chlorpromazine might be of value in therapy of established hæmorrhagic shock. Dogs subjected to experimental shock by bleeding survived significantly longer after being given intravenous injections of chlorpromazine every 15 minutes until reinfused. It was also noted that the flow through the superior mesenteric vein rose progressively during hypotension when chlorpromazine was given. Dr. R. K. Padhi of Saskatoon showed from experiments on dogs that peripheral blood flow is a more significant measure of hæmorrhage than are either the blood pressure or the pulse rate. Dr. W. E. Wilson of Montreal described alterations in peripheral blood flow after frostbite. He had used an indicator dilution method for differential measurement of plasma and total blood flow through a dog forelimb damaged by cold; plasma flow decreased relative to red cell flow in the injured limb.

Dr. W. Feindel of Saskatoon presented case reports on three patients with tardy ulnar nerve palsy who complained of pain in the elbow and forearm with paræsthesiæ. The ulnar nerve was decompressed by slitting the aponeurosis joining the two heads of flexor carpi ulnaris over the swollen nerve; this relieved symptoms satisfactorily, and function gradually returned. Dr. V. Fredette of Montreal had performed swab tests for gas gangrene bacilli in local operating rooms and found large numbers of the anaerobes in inlet and outlet ducts in the air-conditioning system and even on top of the operating lamp.

By a special microscopic technique, Dr. W. R. Harris of Toronto has demonstrated that neutral fat and fatty acids behave differently after injection into the circulation. The former remain in large droplets and plug lung vessels without causing death, whereas fatty acids break up into small drops and fill the capillary bed of the lungs, causing rapid hæmorrhagic consolidation of the lung and death. Maybe fat released in fracture hæmatoma undergoes hydrolysis and the fatty acids released produce the changes in the circulation characteristic of fat embolism.

Dr. Angus McLachlin and his colleagues of London, Ont., reviewed a series of 270 consecutive cases of intertrochanteric fracture of the femur in which they had found fixation by the Moe plate to be satisfactory. The mortality rate for the entire series was 20.7% and the operative mortality rate 18.8%; the commonest postoperative complication was decubitus ulceration (45%). This group feel that the problem of intertrochanteric fractures is not one of obtaining union, but rather of controlling mortality rate.

The afternoon session on Friday was devoted to surgery of neoplastic disease. In reviewing 105 cases of melanoma of the skin seen at the British Columbia Cancer Institute from 1939 to 1956, Dr. John A. Elliot stated that the Institute staff believe that a primary melanoma wihout metastases should be excised widely; where the primary is adjacent to the lymphatic drainage area, e.g. in the groin, excision should be combined with radical lymph node dissection en bloc.

At the Royal Victoria Hospital, Montreal, Dr. David Ballon had seen 100 cases of carcinoma of the larynx in 30 years. The outstanding symptom in intrinsic cancer was some change in the voice; in extrinsic cancer there was some disturbance in swallowing. Fifty-five patients had an extrinsic cancer (inoperable and incurable) and 45 an intrinsic cancer (operable and generally curable). The usual treatment in operable cases was laryngo-fissure and laryngectomy; in inoperable cases x-ray therapy was given. Results in intrinsic laryngeal cancer were very gratifying; 80% of early cases had a normal life expectancy with fair and even good voice.

Dr. E. J. Tabah of Montreal discussed malignant tumours of the paranasal sinuses with special reference to 10 patients subjected to radical surgery. The commonest site of origin of the tumours was the maxillary antrum. In recent years the trend has been towards more radical surgical excision; mortality and morbidity are now low and results of treatment have improved. Dr. W. K. Lindsay of Toronto discussed bone tumours of the maxillo-facial region in children, a very mixed group of both benign and malignant tumours. Wide local surgical excision where feasible without excessive mutilation was usually successful.

The view that the only sound treatment for any parotid tumour is parotidectomy was advanced by Dr. A. L. Murphy of Halifax, N.S., who pointed out the great difficulty in diagnosis of mixed tumours unless the whole tumour be studied. Even so, a high recurrence rate followed removal of the tumour alone. He condemned the use of an electric stimulator in facial nerve dissection. The 1957 Medallist in Surgery of the Royal College of Physicians and Surgeons, Dr. S. C. Skoryna of Montreal, described his experimental studies of systemic factors in development of carcinoma. These included hormonal, immunological, neurogenic, and neurovascular factors. A neoplastic mass develops as a result of the interplay of local and systemic factors, and carcinoma is not therefore an autonomous growth.

On Saturday morning the Division held two concomitant sessions. One was on general surgical problems and the other on thoracic and cardiovascular surgery.

General Surgical Problems.

Dr. C. C. Ferguson of Winnipeg classified the three types of megacolon occurring in infants and children as: (1) Hirschsprung's disease or congenital aganglionic megacolon; (2) megacolon secondary to anal lesions; (3) functional megacolon due to faulty bowel habits. Peranal rectal wall biopsy might be very helpful in diagnosis of congenital aganglionic megacolon and should be done in newborn infants with severe abdominal distension but no typical x-ray changes, or in obscure cases in older children. Hirschsprung's disease should be treated by resection of the aganglionic bowel segment with re-establishment of continuity. Infants with an early and severe form of the disease require a preliminary colostomy or ileostomy with subsequent definitive resection at 12-18 months.

Dr. F. R. C. Johnstone of Vancouver had seen 23 cases of gastrojejunocolic fistula after operation for peptic ulceration, and suggested that excision of the fistula with adequate partial gastrectomy in one stage in good-risk patients was the treatment of choice. In poor-risk patients, a proximal colostomy is very valuable for jejunocolic fistula. Dr. R. M. Levine and his colleagues of Montreal described a technique of immediate eversion of a permanent ileostomy stoma to prevent retraction or prolapse in cases of ulcerative colitis. Observations on 200 shoulder joints at autopsy led Dr. William Anderson of Toronto to stress the similarity which degenerative changes in shoulder joints and periarticular tissues bear to the more familiar sequence of events in the hip.

Dr. A. A. Klass of Winnipeg submitted evidence that the embryological theory of pilonidal suppuration is untenable and that conservative surgery or no surgery at all may lead to a satisfactory termination of the condition. Experiments on dogs by Dr. R. K. Lyon and his associates of Edmonton confirmed the view that posthistaminic gastric ulcers can be prevented by posterior pituitary extract, even though the latter does not influence gastric acidity. Reviewing 75 cases of spinal cord compression caused by epidural malignant tumours, Dr. E. H. Botterell of Toronto and his associates stressed the need for early diagnosis in these cases, so that appropriate surgical treatment followed by systemic treatment could save the patient the disability and suffering resulting from paraplegia.

The importance of epiploic granuloma is that it may simulate generalized carcinomatosis of the abdominal cavity with infiltration into viscera and obstruction. At laparotomy the surgeon may consider the lesion too advanced for surgery, whereas the prognosis is good if the tumour masses leading to obstructional perforation are removed. One variety of epiploic granuloma follows ingestion of foreign bodies, and Dr. W. E. Kunstler and his colleagues of Montreal described three cases due to ingestion of fishbones.

It is now known that not all islet cell tumours of the pancreas produce insulin, but that some are associated with gastric hypersecretion and fulminating peptic ulceration. Dr. W. C. MacKenzie and his colleagues of Edmonton described two instances of these pancreatic neoplasms, in one of which the patient survived a major pancreatic resection. Dr. R. B. Eaton of Moncton, N.B., reviewed 21 personal cases of carcinoma in the region of the head of the pancreas; radical resection was performed in eight cases, a palliative procedure in eight, and five were considered beyond operative relief. Delay in diagnosis was common, and the latter proved difficult even after laparotomy. The most useful sign was a discrete firm mass palpable after mobilizing the duodenum. Resection is considered a justifiable and valuable procedure in many cases of carcinoma of the head of the pancreas.

Thoracic and Cardiovascular Surgery.

Dr. J. C. Callighan and his co-workers of Edmonton described their results in the open-heart surgery of congenital heart disease, using the Lillehei-De Wall pump oxygenator. Dr. R. O. Heimbecker of Toronto described a method of left heart catheterization improved and modified by him and involving the percutaneous puncture of the left atrium and the passage of a small nylon catheter across the mitral orifice into the left ventricle. Drs. L. L. Whytehead and M. B. Perrin of Winnipeg described their experience with congenital anomalies of the great vessels in the thorax and their

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correction. Dr. A. J. Grace of London, Ont., presented a most interesting and instructive paper on pulmonary decortication, and indicated that this is an operation that deserves wider usage. Dr. C. L. Crosby of Regina gave a similarly interesting paper on his experience and conclusions in the management of 35 cases of cystic disease of the lung. He is convinced that such cystic disease is developmental in origin. Dr. G. A. P. Hurley and his co-workers of Montreal presented their very original conception of the therapeutic paradox that results in the bronchial tree, from the intensive and otherwise successful treatment of pulmonary tuberculosis. Illustrative chest roentgenograms and diagrams strengthened their thesis.

SCIENTIFIC MEETING: SATURDAY AFTERNOON

The scientific meeting of the Royal College was held with Dr. R. M. Janes in the chair. The Lecturer in Medicine was Professor W. Melville Arnott of Birmingham, England, 1957 Sims Commonwealth Travelling Professor, who spoke on "Regional Patterns of Blood Flow in Health and Disease". He noted that there had been little attempt so far at obtaining an integrated picture of blood flow in the whole body. For blood flow studies, the Fick equation was basic. This equation could be adapted to any area of the body, and the concept of measuring flow under stress was gaining ground. The cardiac patient does work by extracting more oxygen from the circulation and shutting down the splanchnic flow during severe exercise with dire results to liver function. Similarly renal blood flow is depressed in severe exercise in cardiac patients, and blood flow in the arms during leg exercise is drastically reduced. Thus in cardiac disease the appropriate output during exercise is achieved by a quantitatively abnormal distribution of blood.

The Lecture in Surgery was given by Dr. I. S. Ravdin, John Rhea Barton Professor of Surgery, School of Medicine, University of Pennsylvania, who discussed the subject of gastric carcinoma, indicating its extremely varied clinical picture and course. In a series from his hospital 11% of diagnoses of gastric ulcer later proved to be carcinoma, whereas 37% of cases with a preoperative diagnosis of probable carcinoma were correct. No clinical study will show carcinoma with certainty. Among 309 cases in Pennsylvania, 27 had been found inoperable, 180 resectable, 111 had a curative resection and 57 a biopsy and 45 palliative procedure. Of the 111 curative resections, 54 were on cases with positive lymph nodes. Thus the truly curable cases with negative lymph nodes comprised 18.4% of the total. The operative mortality for all operations was 6.7% and for curative resection 0.9%. The total five-year survival was 15.5%, but for curative resections with negative lymph nodes 50%. One patient survived after a simple biopsy and two after a palliative operation.

At the convocation of the Royal College later in the afternoon the newly admitted fellows were presented. Honorary fellowships were awarded to Professor W. Melville Arnott and Dr. I. S. Ravdin. The medicine and surgery medals were awarded to Dr. R. D. Rowe of Toronto and Dr. S. C. Skoryna of Montreal respectively, and diplomas were presented to the two lecturers.

SECTION OF OBSTETRICS AND GYNÆCOLOGY

On Friday afternoon the section of obstetrics and gynæcology held two panel discussions, with Dr. George Maughan of Montreal in the chair. The first discussion was on the paradox of fetal anoxia—the obstetrician's responsibility? The panel, which consisted of Dr. J. L. Macarthur, Montreal, Dr. W. M. Paul, Toronto, Dr. R. M. Parsons, Toronto, Dr. A. Ross, Montreal, and Dr. J. P. Robb, Montreal, considered means of reducing neonatal morbidity and mortality, which are still too high. The person responsible for resuscitation should be the one best informed on the respiratory physiology of the newborn in each hospital. Machines blowing oxygen into the lungs under high positive pressure were condemned; they would blow a hole in the tissue before expanding the alveoli. The importance of a clear airway was emphasized. It was noted that anoxia could be grouped into two classes: (1) abrupt, leading to death or rapid cerebral damage; (2) slowly increasing anoxia *in utero*, eventually reaching a critical level. The effects included mental retardation (behaviour problems, reading disability), motor abnormalities and focal epilepsy.

The present status of bacterial infections in gynæcology was discussed by Dr. W. H. Allemang, Toronto, Dr. J. R. Boyd, Vancouver, Dr. D. C. McEwen, Regina, Dr. F. J. Tweedie, Montreal, Dr. K. J. R. Wightman, Toronto, and Dr. Gertrude Kalz, Montreal. Bacterial infections considered included wound infection, severe gynæcological infection, and pelvic tuberculosis. It was pointed out that tuberculosis appears to be on the increase in Canada and that the once dreaded infection with streptococcus A is now the easiest to manage. Nasal carriers are of importance to gynæcological infection, therefore nasal swabbing should be always used. Not all Clostridia are dangerous; they need specific conditions to cause gas gangrene. Diagnosis of the latter must be clinical, and treatment with large doses of gas gangrene antitoxin should begin before laboratory confirmation. The serious manifestations of staphylococcal infection nowadays are staphylococcal pneumonia and enteritis due to use of antibiotics. Broad-spectrum antibiotics are bacteriostatic rather than bactericidal, and of little value in prophylaxis. Gynæcological wound infections seem more common nowadays, with the commonest invader the staphylococcus (80-90%).

AMERICAN HEART ASSOCIATION

The 30th scientific session of the American Heart Association, held in Chicago, October 25-28, 1957, commemorated the Tercentenary of William Harvey; during the entire program frequent allusions were made to his monumental work. In addition, throughout the sessions, a medical motion picture entitled "William Harvey and the Circulation of the Blood" was shown, and most of the physicians availed themselves of this opportunity. The film was in colour and sound, and was prepared for the Royal College of Physicians of London. In it much of Harvey's experimental work, later published in "De Motu Cordis", was recaptured on film. Its preparation was under the able supervision of Sir Henry Dale and others.

Other valuable educational films shown included "Open Operation for Aortic and Pulmonic Stenosis" by Dr. Henry Swan; "Disorders of the Heart Beat", an excellent exposition of various cardiac arrhythmias; "Tetralogy of Fallot", emphasizing both medical and surgical aspects, and depicting the Blalock method of correction; "Anatomic Correction

of the Tetralogy of Fallot Defects under Direct Vision, Utilizing the Pump Oxygenator"; "Movements of the Valves of the Heart and the Origin of the Heart Sounds", a most instructive film.

The first day was divided between two concurrent symposia, one on heart sounds and murmurs, and the other on the prevention and treatment of cardiac emergencies. The symposium on cardiac emergencies included discussions involving pregnancy, pædiatrics and anæsthesia, surgery, drug therapy and anxiety states.

The symposium on heart sounds and murmurs consisted of short presentations followed by discussion periods. The first group of presentations was on mechanisms of cardiovascular sound, and included studies by hæmodynamic, phonocardiographic and radiologic methods, either singly or in combination.

The second group of presentations involved the clinical aspects of auscultatory phenomena, and included discussions of mitral stenosis, splitting of heart sounds, "mammary souffle", and systolic murmurs in general.

The evening session on October 25 was limited to instrumental methods in cardiovascular diagnosis, and included papers on cardiac catheterization (left and right), phonocardiography, electrocardiography, angiocardiography, electrokymography, *intracardiac* phonocardiography, indicator (dye) dilution curves, oximetry and cinefluorography. There was a great deal of discussion from the floor, and it was especially interesting to note that some of this discussion was initiated by physicians who began their own researches into heart sounds some years ago, and are now having their conclusions verified instrumentally. Outstanding among these were Samuel A. Levine of Boston and Harold N. Segall of Montreal.

On Saturday, October 26, a general scientific session was held, which lasted the entire day. Concurrently, however, four separate and distinct simultaneous scientific sessions were in progress consisting of a session on basic science, a session on circulation, a session on clinical cardiology and a session on rheumatic fever and congenital heart disease. The morning opened with an American Heart Association award to Drs. André Cournand, Dickinson Richards, Jr., and Werner Forsmann (in absentia), for their pioneering work in cardiac catheterization. This was followed by a series of miscellaneous papers on hypertension, dye dilution curves, rheumatic fever, and surgery for congenital heart disease, and the morning was closed by the Lewis Conner Memorial Lecture on rheumatic heart disease by Charles H. Rammelkamp, Jr. Dr. Rammelkamp, an extremely dedicated gentleman, pointed out several ways in which the practising physician can aid in decreasing the incidence of rheumatic fever.

The simultaneous scientific sessions on Saturday afternoon ranged widely from the most practical applications of cardiovascular surgery to the most fundamental conceptions of cardiac anatomy and physiology. To skim the cream off these simultaneous sessions was an exercise in logistics involving split-second timing in leaving one auditorium at the end of one paper, and arriving at another auditorium in time to hear a valuable paper on an entirely different subject. By the end of the day this reporter had become expert in this particular form of cream-skimming. Subjects discussed included coronary flow and oxygen metabolism, computation of cardiac work, the detection and estimation of the magnitude of aortic regurgitant flow, comparison of sympathomimetic amines, Wolff-Parkinson-White syndrome, the first heart sound in mitral stenosis, detection of left-to-right shunts by a nitrous-oxide method, indicator-dilution curves in mitral stenosis and insufficiency. Many of the papers described different methods for measuring the same abnormalities, and in certain cases discussion between the speakers and those in the audience waxed hot. However, the tension was admirably dissipated by the remark by one of the speakers, "There's room for all of us, fellows."

On Sunday morning, October 27, the program opened with the general scientific session. This included papers of such varying flavour as changes in blood cholesterol, and circulation and respiration in the giraffe. The morning sessions closed with the George E. Brown Memorial Lecture, "Current Evaluation of the Thrombosis Problem", by Dr. Nelson W. Barker of the Mayo Clinic.

The afternoon session opened with the presentation of the Albert Lasker Award (a statuette of the Winged Victory, a bound citation and $2500.00). This year's winner was Dr. Isaac Starr of Philadelphia, who responded with a charming little presentation in which he paid tribute to all those who had helped him during his professional life. Particularly intriguing was Dr. Starr's special tribute to his wife, who, he said, "has never evinced the slightest desire for either a mink coat or a Cadillac". Following this, papers presented included several on the newer concepts of lipid metabolism in atherosclerosis, one on phonocardiography, and an extremely interesting medical motion picture on postero-medial annuloplasty of the mitral valve for mitral insufficiency. This operation was performed under direct vision, utilizing a pump-oxygenator, and exemplifies the type of surgery of the heart we should be expecting during the next few years.

Monday morning, October 28, was occupied by two simultaneous scientific sessions, one on cardiovascular surgery and the other on hypertension. The former leaned heavily in the direction of description of various types of pump-oxygenators for open cardiac surgery and of various types of surgical procedures for the correction of different congenital and acquired cardiac abnormalities. The latter concerned itself with several apparently unrelated aspects of the clinical and experimental investigations of high blood pressure, and no specific trend could be discerned. One fears that there are to be no surprises in the 1957-58 hypertension season.

In general, however, one specific trend could be noted in the papers in general. As each investigator

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becomes more and more familiar with and adept in the particular method of cardiovascular investigation he has chosen, the tendency has been to apply that method more and more broadly, and finally to exclude all other methods of investigation from a position of importance in any particular form of cardiovascular disease. For example, an uncritical observer would perhaps accept the intracardiac phonocardiograph as the ultimate tool in the diagnosis of all forms of congenital and acquired heart disease. An equally uncritical but oppositely biased investigator or observer might award that distinction to the indicator dilution technique. In other words, there is a tendency for each worker to ride his own hobby-horse and to forget perhaps that the diagnosis and treatment of heart disease usually, if not always, requires all the means, whether clinical or instrumental, that have been placed at our disposal or will so be placed for some time to come. S.J.S.

PUBLIC HEALTH

INFLUENZA VACCINATION IN THE U.S.A.

The U.S. Public Health Service issued on November 1 the following statement on Asian influenza vaccinations:

"As announced on October 23, industry is now undertaking to produce Asian strain vaccine which is somewhat more effective than the present vaccine in the prevention of the illness. Specifically, the change being made is from a vaccine containing 200 CCA units (CCA is an abbreviation for chicken cell agglutination units which are a measurement for the inactivated viral content of a given volume of vaccine fluid) to 400 CCA units providing an increased level of protection.

"All manufacturers of Asian strain influenza vaccine are expected to be in production on the higher potency vaccine by December 1, with some of the new vaccine expected to be released within the next few weeks. Those who have already received the presently available vaccine have received a substantial degree of protection against Asian influenza.

"The Public Health Service recommends the following with respect to dosage:

"1. As the 400 CCA Asian strain influenza vaccine becomes generally available, it is recommended that for those who have not been vaccinated, the new vaccine be used in a single 1.0 c.c. dose injected under the skin (subcutaneously), except in young children, for whom two injections between the layers of the skin (intracutaneously) are recommended, given in 0.1 c.c. amounts at an interval of a week.

"2. For (a) those who have already received a 0.1 c.c. dose intracutaneously of the 200 CCA vaccine, and for (b) those who have received a 1.0 c.c. dose subcutaneously of 200 CCA vaccine, and who are in special risk groups—namely, pregnant women, the aged, and those suffering from certain chronic ailments such as rheumatic heart disease and pulmonary illnesses—it is recommended that a second 1.0 c.c. subcutaneous dose of 200 CCA vaccine or 0.5 c.c. of 400 CCA vaccine be given in not less than two weeks after the first dose.

"3. Physicians may wish to recommend a second injection, as well, for other patients under their care."

LETTERS TO THE EDITOR

NOT ENOUGH BODIES

To the Editor:

In conversations with my colleagues in practice, I have been dismayed to find that many are not aware of perhaps the greatest threat to the quality of medical education today. This is the insidious development of a shortage of cadavers for teaching and research. Nowhere is this shortage more serious than in Ontario, which produces the greatest number of medical graduates. With rumours flying about proposals to open new medical schools in Ontario, one wonders where adequate numbers of bodies are to be obtained.

Of course, the remedy is not to delay the opening of new schools that everyone concedes are needed, but to greatly increase the number of cadavers provided for anatomical studies. In Ontario, the Anatomy Act at first glance appears to be adequate insurance of a good supply. It specifically states that bodies not claimed for burial within 24 hours by a relative or *bona fide* friend must come under the control of the local inspector of anatomy who will assign it to a department of anatomy. No dissection may be done for a further 14 days, allowing late claimants a very considerable period of grace. Coroners and officials of morgues, hospitals, etc., must, under the Act, notify their inspector of any unclaimed bodies within 24 hours.

Now, even the most disinterested physician will agree with me that these provisions are generally unknown or deliberately ignored. In most cases the physicians or officials in charge do not know the law. Moreover, they often join their efforts to those of clergymen and service-club executives to force honest but misguided officials to unlawfully spend public funds to bury indigents, thinking all the while that their action is humane and correct. They most certainly do not know that every time they deprive a medical school of an unclaimed body they are aggravating a serious problem.

My plea is particularly directed to physicians in Ontario, but physicians in the other provinces should be aware that similar situations exist in them. Whenever a physician knows that an unclaimed body lies in any morgue for more than 24 hours, he should notify the local inspector of anatomy. Local inspectors (who are coroners with the additional

title) are found in most of the towns and cities. When in doubt, a physician can get advice by telephone from the closest Anatomy Department, which would be glad to oblige.

A further way in which physicians might help is by educating the public, hospital authorities and provincial legislators. The public must be told of the threat to the quality of medical education caused by the indiscriminate burial of unclaimed bodies. Every time the officials of a community bury an indigent without the express permission of the inspector of anatomy, not only are they breaking the law but they are lowering the quality of medical education. The public is the inevitable loser.

Finally, attention might be directed to the fact that most British and some American schools receive a great number of bodies by bequest. Although by common law, one's body after death is the "property" of the nearest relatives, the wishes of the deceased, if known by the relatives, lawyer and clergyman, are generally carried out. Although wills are usually read after a burial, those who wish to have their bodies used for the advancement of humanity should specifically state their wish in their will, not neglecting to notify their close relatives, clergyman, etc. I would be pleased to provide any interested physician or layman with appropriate information.

In closing, I would like to emphasize that this is not a problem for anatomy professors only. Physicians, lawyers, clergymen, public officials, and the public at large are intimately involved. False ideas of propriety must not obscure this fact.

J. V. BASMAJIAN, M.D.

Professor and Head, Department of Anatomy,
Queen's University,
Kingston, Ont.,
October 28, 1957.

CANADIAN FEDERATION OF BIOLOGICAL SOCIETIES

To the Editor:

The Board of the Canadian Federation of Biological Societies has requested me to inform you of the formation of this Federation in Ottawa on October 11, 1957. The Federation comprises four member societies: the Canadian Physiological Society, the Pharmacological Society of Canada, the Canadian Association of Anatomists, and the Canadian Biochemical Society. The Canadian Physiological Society has been active since 1935. The other three societies have been founded in the past two years; many of their members already belong to the Canadian Physiological Society. However, the rapid growth of these sciences has made it desirable to form societies for the individual disciplines not only to further their development in Canada but also to meet international obligations.

In accordance with the terms of its Constitution, the Canadian Federation is managed by a Board on which each constituent society has two representatives. The purposes of the Canadian Federation are to bring together persons who are interested in teaching and research in the biological sciences, to disseminate information on the results of biological research through scientific meetings and through publication, to encourage exchange of information between constituent societies, and to act for the member societies when it is agreed that concerted action is desirable.

At the kind invitation of Queen's University, the Canadian Federation of Biological Societies will hold its first annual meeting in Kingston, Ont., in June 1958.

E. H. BENSLEY, M.D.,
Honorary Secretary to the Board,
Canadian Federation of Biological Societies.
Montreal General Hospital,
Montreal 25, Que.,
October 31, 1957.

HÆMOLYTIC DISEASE OF THE NEWBORN

To the Editor:

In your editorial comment (*Canad. M. A. J.*, 77: 704, 1957) on hæmolytic disease of the newborn attention was drawn to the work of Walker and Mollison[1] in England, who have shown that the infant death rates due to hæmolytic disease had only fallen from 0.8 to 0.6 and not to 0.2 per 1000 live births, the theoretical irreducible minimum. An analysis of the returns for this country (Table I—obtained from the Dominion Bureau of Statistics through the kindness of Dr. Jean F. Webb) for the years 1950-1956 (inclusive) reveals that these infants fare no better in Canada as a whole than in England.

TABLE I.—INFANT MORTALITY RATE PER 1000 LIVE BIRTHS FROM HÆMOLYTIC DISEASE, CANADA BY PROVINCE, 1950-56

	1950	*1951*	*1952*	*1953*	*1954*	*1955*	*1956*
Newfoundland	0.76	0.43	0.56	0.63	0.59	0.20	0.89
Prince Edward Island		0.75	0.37	1.10	0.73	0.72	2.26
Nova Scotia	0.52	1.11	0.72	0.98	0.85	0.53	0.63
New Brunswick	0.98	0.62	1.26	0.55	0.78	1.02	1.03
Quebec	1.14	1.12	1.31	1.13	1.21	1.24	1.05
Ontario	0.61	0.79	0.82	0.74	0.70	0.62	0.47
Manitoba	0.52	0.25	0.34	0.71	0.67	0.54	0.32
Saskatchewan	0.93	0.74	0.62	0.46	0.72	0.44	0.58
Alberta	0.66	1.07	0.62	0.61	0.57	0.44	0.74
British Columbia	0.55	0.82	0.60	0.44	0.52	0.62	0.77
Canada	0.81	0.88	0.91	0.81	0.84	0.78	0.74

It is probable that some deaths due to hydrops and kernicterus are being incorrectly ascribed to hæmolytic disease and if this is so the mortality rates due to the latter condition will be less than the figures would suggest. When the mortality rates for the individual provinces are compared, it is seen that these are lowest and the survival rate is highest in Manitoba. This would suggest that the antenatal detection of the disease and the standard

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of postnatal care may be higher in this province than in any other. Whether this is so or not, a more detailed review of the results of treatment of infants with erythroblastosis than is given in the above table should be undertaken with a view to improving the over-all results of treatment in Canada.

J. W. GERRARD, D.M., M.R.C.P.,

Professor of Pædiatrics,
University Hospital,
Saskatoon, Saskatchewan,
November 5, 1957.

REFERENCE

1. *Lancet*, 1: 1309, 1957.

THE LONDON LETTER

(From our own correspondent)

GOLDEN JUBILEE

In 1907 the Royal Society of Medicine, formed by the amalgamation of some 14 medical societies, came into being and received its Royal Charter. To celebrate the jubilee of this auspicious event in the history of British medicine the Society held a banquet last month, at which due tribute was paid to the tremendous progress that the Society has made in the intervening years. Perhaps its greatest attribute is its library, which now ranks as one of the great medical libraries of the world. Like all voluntary organizations in a modern "Welfare State", however, it is finding it increasingly difficult to lay its hands upon the wherewithal with which to maintain the progress which any live organization must do if it is to continue to subserve a useful function. The challenge is being met with vigour and enthusiasm, and the Society has every justification for facing the future with sober optimism.

VISCOUNT NUFFIELD

One of the most pleasing features of the banquet was the presentation to Lord Nuffield of the honorary fellowship of the Society. Only a week before the eightieth birthday of this munificent benefactor of medicine had been celebrated by the announcement that the Nuffield Foundation had presented a sum of £80,000 for the endowment of a chair of child surgery at the Institute of Child Health and The Hospital for Sick Children, Great Ormond Street. This is the first chair of child surgery in this country, and is a worthy accompaniment to the chair of child health at the Institute which the Foundation endowed in 1944. Medicine has always been the main recipient of Lord Nuffield's generosity, though other deserving causes have not been neglected, and his total gifts to these amount to over £27 million.

FLEMING MEMORIAL

On October 12, a memorial to Sir Alexander Fleming was unveiled at his birthplace, Lochfield farm in Ayrshire. The memorial is a three-ton block of Cumberland granite, bearing the simple inscription: "Sir Alexander Fleming, Discoverer of Penicillin, was born here at Lochfield on 6th August, 1881".

MORTALITY STATISTICS

The effect of the aging population is well brought out in a report just published by the Registrar General, based upon the provisional figures of causes of death in 1956. These show that of the 74,790 deaths from coronary disease and angina, 25,469 were of persons aged 75 and over. An interesting feature of the report is a table showing the loss of expected years of life due to mortality from certain causes. In 1956, the loss of years of working life for every 10,000 men in the working age period, 15 to 64, was: 114 for cancer, 113 for heart disease, 87 for accidents, and 80 for bronchitis and pneumonia. The corresponding figures for women were 97, 50, 25, and 42. The number of deaths from suicide was 5282, the highest ever recorded; 2520 of them occurred between the ages of 45 and 65 (1461 men and 1059 women).

HELPING THE GENERAL PRACTITIONER

Work is to begin shortly on the first diagnostic centre for general practitioners to be provided in this country. It is to be built in Edinburgh as a self-contained unit providing facilities for a wide range of diagnostic procedures for 100 general practitioners. These will include a laboratory and x-ray and electrocardiographic equipment, which will enable practitioners to deal with many types of cases which otherwise would need to be referred to hospital out-patient departments. The family doctors in the area it will serve will be able to meet by appointment at the Centre any of their patients who require special investigation or follow-up. A senior physician will act in an honorary capacity as medical adviser in appropriate cases.

London, WILLIAM A. R. THOMSON
November 1957.

FORTHCOMING MEETINGS

UNITED STATES

PAN AMERICAN ASSOCIATION OF OPHTHALMOLOGY, 5th Interim Congress, New York, N.Y. (Dr. William L. Benedict, 100 First Avenue Building, Rochester, Minnesota.) February 1, 1958.

INTERNATIONAL COLLEGE OF SURGEONS, 11th Biennial Congress, Los Angeles, California. (Dr. Karl A. Meyer, Secretary, 1516 Lake Shore Drive, Chicago 10, Illinois.) March 9-14, 1958.

OBITUARIES

DR. HENRY WATTERS DUNNET, 70, who had practised at Avonlea, Sask., for 45 years, died in Regina on October 3. Dr. Dunnet was born in Ottawa, and graduated from McGill University in 1910. After doing postgraduate work in Edinburgh and Glasgow he returned to Canada and for some time was superintendent of an Ottawa sanatorium. He also practised for a short time at Lethbridge, Alta., before going to Avonlea. In gratitude for his service to them for many years, 1000 residents of the district gathered in Avonlea on June 27, 1949, and declared the day in honour of Dr. Dunnet.

He is survived by his widow and three daughters.

DR. HAROLD S. ELLIS, 57, a practitioner in the Eastern Townships, Que., died on October 19. He graduated in medicine at McGill University in 1931 and afterwards did postgraduate work in Boston. He practised in Magog for some years before moving to Sherbrooke. In recent years his practice had been almost entirely in surgery. Dr. Ellis played a part in the planning and equipping of the new Sherbrooke hospital and was a former chairman of the medical board and a governor and life member of the corporation. He was also district medical officer for Canadian National Railways.

Dr. Ellis is survived by his widow and a daughter.

DR. GAETAN LEPINE, 50, a well-known physician in Quebec City, died suddenly on September 26. He was born in St. Sauveur, Que., and graduated in medicine from Laval University in 1933. He practised at St. Ubald until 1945.

Dr. Lépine is survived by his widow, two sons and two daughters.

DR. ORMOND OSCAR LYONS, 66, who had practised in British Columbia for 39 years, died in Vancouver on October 9. He was born in Waterford, N.S. In 1917 he graduated from McGill University and in the following year moved to Port Alice, B.C. He went to Vancouver in 1924 as C.P.R. doctor and four years later moved to Powell River where he held hospital appointments as chief physician and surgeon. In 1948 he returned to private practice in Vancouver.

Dr. Lyons is survived by his widow, a son and three daughters.

DR. DONALD W. McDONALD, an eye specialist in Montreal, died in the Montreal General Hospital on October 12. Dr. McDonald was born in Glace Bay, N.S., and graduated from Dalhousie University, Halifax, in 1932. During World War II he served with the RCAF. He held the post of associate ophthalmologist at the Montreal General Hospital and was on the staff of McGill University.

Dr. McDonald is survived by his widow, a son and a daughter.

DR. GILBERT J. McMURTY, 64, a well-known physician in Regina, Sask., died on September 20. Dr. McMurty graduated in arts from McGill University before serving in the First World War. After the war he returned to McGill to study medicine and later did postgraduate work in Vienna where he specialized in ophthalmology and otolaryngology. In 1924 he went to Regina, where he practised until his retirement two years ago.

Dr. McMurty is survived by his widow, a son and a daughter.

DR. SYDNEY E. SPARLING, 49, who was medical adviser to the Canadian Pension Commission in Ottawa, died on October 20. He was born at Lindsay, Ont., and graduated in 1933 at the University of Toronto. He practised at Owen Sound, Ont., until the outbreak of World War II when he enlisted in the RCAF. After the war Dr. Sparling joined the Department of Veterans Affairs. He was the medical representative on the first board of the Victorian Order of Nurses and maintained his interest in the work of the Order in Ottawa.

Dr. Sparling is survived by his widow.

DR. JOSEPH ROMAIN TITTLEY, 50, who was a former professor of internal medicine at the University of Ottawa, died suddenly at his home in Ottawa on October 11. He graduated in medicine from the University of Montreal in 1934. He practised in Alfred and later in Eastview, Ont., before moving to Ottawa in 1952. Dr. Tittley was associated with the Ottawa General Hospital and had been a professor of medicine at the University of Ottawa since the organization of the medical school. He was a member of the Canadian Arthritis and Rheumatism Society and a founder and past president of la Société Médicale de l'Outaouais.

Dr. Tittley is survived by his widow, two sons and a daughter.

DR. GEORGE G. WANNOP, 70, an Edmonton physician who was formerly a medical missionary in China, died in Edmonton, Alta., in October. During World War I he served with the 10th Field Ambulance. He graduated from the University of Manitoba in 1919 and until 1926 served as superintendent and chief surgeon at the Canton Mission Hospital in China. After his return to Canada he practised at Red Deer, Alta., and at Wetaskiwin and Lethbridge. In 1940 he became officer commanding the 17th Field Ambulance and later commanded the Vernon Military Hospital and the Victoria Military Hospital. After the war he opened a practice in Edmonton. On his retirement in 1954 he joined the Northern Health Services.

Dr. Wannop is survived by his widow and a son.

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PROVINCIAL NEWS

SASKATCHEWAN

The Fiftieth Annual Meeting of the College of Physicians and Surgeons of Saskatchewan and the Saskatchewan Division of the Canadian Medical Association was held in Moose Jaw during the week of October 7. This meeting combined clinical, business and social sessions.

A pre-convention coffee party was held at the Grant Hall Hotel on the evening of October 7, when those in attendance were the guests of the Council of the College and the Moose Jaw and District Medical Society.

Clinical and business sessions were held at the Moose Jaw Training School. Dr. G. D. G. Howden, President of Council, chaired the business sessions.

Dr. Peart, the Assistant Secretary of the Canadian Medical Association, addressed the members at the luncheon on October 8, and Dr. Morley Young, President of the Canadian Medical Association, was a guest speaker at the College dinner on the same date. On Tuesday afternoon scientific presentations were made by Dr. H. Harrison of Edmonton and Dr. J. G. Stratford of Saskatoon, and Dr. L. V. Ackerman of St. Louis, Missouri, gave the Munroe Lecture. The Munroe Lecture is arranged annually through the courtesy of the Saskatchewan Division of the Canadian Cancer Society in memory of the late Dr. F. D. Munroe. The guest speaker at the Wednesday luncheon was the Honourable Walter Erb, Minister of Public Health in the Government of Saskatchewan. The Ritchie Cup Dinner was held on Wednesday evening in the Temple Gardens with Dr. L. G. Bray, the President of the Moose Jaw and District Medical Society, as chairman. The Saskatoon and District Medical Society won the Ritchie Cup, and Dean J. W. Macleod received a new award established in memory of the late Dr. Robin Dale. Dean Macleod's award was made by the judges to the best actor. The afternoon of Wednesday, October 9, was devoted to the meetings of the various sections of the College.

On Thursday, October 10, the clinical sessions consisted of a film on cardiac surgery by Professor E. M. Nanson, of the University of Saskatchewan, a paper by Dr. R. C. Harrison of Edmonton, a panel on staphylococcus infection in the hospital, a paper by Dr. Stuart Houston of Yorkton, and a clinic on endocrine problems by Dr. Donald Wilson of the University of Alberta.

In the evening a smorgasbord dinner was held at the Moose Jaw natatorium.

On the morning of Friday, October 11, two panel discussions were held, one on the problems presented by compulsory and voluntary prepaid medical care plans, and one on hospitalization. At noon a very successful beefsteak barbecue was sponsored by the Moose Jaw District Medical Society at the Armories. In the afternoon a competition for the golf cup was held at the Willowdale Golf Course. This was won by Dr. D. F. McAlpine of Regina.

At the Golden Jubilee meeting of the Saskatchewan Division of the Canadian Medical Association, held in Moose Jaw from October 8 to 11: Dr. A. F. W. Peart, Dr. G. D. G. Howden (Division President), and Dr. M. A. R. Young, with friend.

C. E. Barton, Assistant Superintendent of the General Hospital in Regina, was elected President of the Saskatchewan Hospital Association for 1957-58 at the close of the Association's 39th Annual Convention held the week of October 14. Mr. N. Kushnir of Kenora Union Hospital was elected Vice-President.

G. W. PEACOCK

MANITOBA

In an address before 500 members of the Winnipeg Horticultural Society on October 9, Dr. H. V. Waldon of Vita suggested that the beautiful fireweed which grows in all ten provinces be recognized by Order of Council as the national flower of Canada.

Professor J. Z. Young, F.R.S., Professor of Anatomy at University College, London, addressed the medical students and staff of the University of Manitoba on October 18 on "Some aspects of cellular organization".

ROSS MITCHELL

ONTARIO

Ontario's hospital insurance plan will become effective January 1, 1959. The plan will cost an estimated $210,000,000 in the first year, to be divided between Ottawa and the province. Ottawa's share will be $74,000,000 and Ontario's $136,000,000 of which the province hopes to raise half through premiums. At the outset those working for firms with 15 or more employees must join and will pay through payroll deductions. Others may contribute voluntarily. Benefits include public ward hospital care, regular nursing services and various in-patient hospital services. Out-patients will be covered for emergency treatment within 24 hours of an accident. Tuberculosis and mental hospital treatment is covered; the Federal government does not share in these costs.

The compulsory feature is expected to give the program an immediate membership of more than

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3,500,000 with the expectation that by the end of the first year there will be 5,000,000 members. The monthly premium for a single person will be $2.10; the family cost will be $4.20, including eligible dependent children up to 18 and any unmarried son or daughter who is over 18 and who is dependent on the family because of physical or mental disability. The province will pay the premium for social assistance cases whose inability to pay has been demonstrated by a means test.

The plan provides for unlimited stay in hospital, regardless of age, pre-existing conditions, or occupation. There will be no waiting period for benefits by those groups for whom membership in the plan is mandatory. Those who do not take advantage of the opportunity to enrol before the plan commences will be required to pay premiums for six months before becoming eligible.

An introductory law course for doctors has been arranged by the Medico-Legal Society of Toronto and will be held on 14 alternate Wednesday evenings. Sixty physicians have registered. Among the lectures to be given are: "The doctor's position in furnishing information" by J. D. Hilton, Q.C.; "The liability of hospitals" by Edson L. Haines, Q.C.; "The rules of evidence" by Hon. Mr. Justice G. A. Gale; "The expert witness" by Hon. Mr. Justice C. D. Stewart; "The assessment of damages in personal injury cases" by Isadore Levinter, Q.C.; "Adoptions and disputed paternity proceedings" by John T. Weir, Q.C., and John W. Brooke; "Doctors and wills" by Terence Sheard, Q.C.; and "The doctor and criminal law" by H. H. Bull, Q.C., W. B. Common, Q.C., and G. A. Martin, Q.C.

Dr. Murray A. Woodside has discontinued practice in Ottawa to accept an appointment as Assistant Medical Director of the North American Life Assurance Company in Toronto.

Dr. Jack Kaufman, cardiologist, Harper Hospital, Detroit, addressed the Essex County Medical Society at their October meeting, on "Cardiac complications in pregnancy".

Dr. Peter Kerley, director of the department of diagnostic radiology, Westminster Hospital, London, consultant radiologist, National Heart Hospital, and consultant radiologist, Ministry of Health of Great Britain, visited Toronto after attending a meeting of the American Roentgen Ray Society in Washington at which he was a guest speaker. He attended medical rounds at Sunnybrook Hospital and radiological rounds at the Toronto General Hospital. He addressed the Ontario Association of Radiologists on "Radiation hazards in diagnostic radiology", and through the Division of Post-Graduate Studies of the Faculty of Medicine gave a lecture on "Pulmonary changes in acquired and congenital heart disease".

The Ontario Division of the Canadian Diabetic Association has elected these officers: President, Mr. A. V. Holland, London; Vice-President, Mrs. Gordon Hall, Kitchener; Secretary, Mr. W. M. Paterson, London. Members of the medical advisory committee are Dr. Hugh T. McAlpine, Dr. John C. Rathbun and Dr. E. M. Watson, London; Dr. James Tice and Dr. H. R. McAlister, Hamilton; Dr. W. W. Snelling, Welland; Dr. Lloyd Thompson, Peterborough; Dr. Arthur J. McGanity, Kitchener; and Dr. Wallace Troup, Ottawa.

Dr. Richard D. Rowe, Hospital for Sick Children, Toronto, has been awarded the gold medal of the Royal College of Physicians and Surgeons of Canada for his work on the hæmodynamic changes in the pulmonary vessels of infants. Dr. Rowe showed that these pressure changes were completed about ten days after birth.

The twelfth annual graduate course presented by the Medical Alumni Association of the University of Toronto had as its theme emergencies in practice. About 450 members registered for the three days of lectures, round table discussions and case presentations held at Sunnybrook and Toronto General Hospitals.

Dr. William Boyd delivered the Medical Alumni oration. His topic was the spontaneous regression of cancer. He described rare cases of complete and permanent spontaneous recovery from cancer; these cases had received either no treatment or treatment admitted to be completely inadequate. There is no reason to suppose that cancer cells become weak and die, any more than when a person recovers from tuberculosis without treatment it is because tubercle bacilli causing the disease have ceased to multiply. In both instances recovery must be attributed to resistance on the part of the tissues of the body, that is, immunity. We are only on the threshold of the study of immunity against cancer.

Dr. Boyd was made an honorary life member of the Medical Alumni Association.

Dr. Tom Robson has been appointed chairman of a committee of the Essex County Medical Society which is to study the requirements of a proposed Faculty of Medicine at Assumption University.

The nursing division of the Ontario Department of Health is introducing a new evening course for certified nursing assistants. The classes will be given on two evenings a week and for a full day on Saturdays. Towards the latter part of the course there will be a concentrated block of four months' supervised hospital experience. The course is open to persons over 17 years of age with a grade eight education or its equivalent. Since the nursing assistant program was inaugurated in 1946, 2800 assistants have been certified. They have now become a recognized part of the nursing team working under supervision of professional nurses and doctors, in hospitals, institutions and private homes.

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In 1956 there were 221 deaths in Ontario from tuberculosis. This is a rate of 4.1 per 100,000 population, the lowest in Canada. In the 60-69 year group there were 45 male deaths and seven female deaths and in the over-70 group there were 51 male and nine female deaths. After the age of 50 the tuberculosis death rate rises sharply.

LILLIAN A. CHASE

The Medical Historical Club of Toronto met on October 25 with Dr. J. W. Scott, the president, in the chair. Dr. Joseph Daly read a paper on John Elliotson (1791-1868), an Edinburgh graduate, who was professor of medicine at the newly founded University College, London, until his dabbling in animal magnetism and demonstrations of mesmerism compelled his resignation. In spite of this, Elliotson, who was born and died in London, was subsequently restored to favour and asked to give the Harveian Oration in 1846; he was the first to give this in English.

On Saturday, October 19, a plaque was unveiled in Bond Head to honour the memory of Sir William Osler in his native town. There were a number of distinguished speakers and the plaque was unveiled by Dr. G. L. Blackwell and dedicated by the Reverend C. R. P. Hearn.

A special clinic for low vision patients, jointly sponsored by the University of Toronto and the Canadian National Institute for the Blind, has been established under the direction of Dr. D'Arcy Macdonald of the Department of Ophthalmology, University of Toronto and Toronto Western Hospital. This clinic is held in the out-patient eye clinic at the Toronto Western Hospital. Patients may be seen by referral from the C.N.I.B. or from ophthalmologists.

NEW BRUNSWICK

Dr. George L. Dumont of Campbellton has been elected President of l'Association des Médecins de Langue Française du Canada. Other officers include Dr. Jean Paul Carette and Dr. François St. Laurent, both of Campbellton.

Dr. Lachlan MacPherson has been appointed superintendent of the Saint John Tuberculosis Hospital to succeed Dr. R. J. Collins, who retired from the position on October 1. Dr. Collins had been superintendent of the hospital since 1930, during which period the hospital has been expanded and the treatment of tuberculosis has changed remarkably. On retirement, Dr. Collins was honoured at a reception by the commissioners, staff and medical consultants of the hospital, all of whom joined in recounting the services of a doctor dedicated to the treatment and rehabilitation of patients suffering from the scourge of tuberculosis. Dr. Collins, in his address, stressed that although tuberculosis was under a degree of control, further efforts for a long period will be necessary to maintain the gains already made.

Dr. Collins received an unusual number of professional honours and also served well in community efforts.

Dr. MacPherson, his successor, has served a long and distinguished apprenticeship in tuberculosis treatment and is a very happy choice to act as chief in the excellent hospital in Saint John.

Dr. H. L. Logan has retired from the position of District Medical Health Officer for the counties of Kings, Queens and Sunbury. He served in Sussex from 1934, with time out for services overseas in World War II. Dr. Logan was guest of honour at a testimonial dinner sponsored by the health staff and other friends in Sussex, N.B.

In the first week of October the Maritime Association of Psychiatrists held their Annual Meeting in Saint John, N.B. Dr. R. D. Nixon of Saint John presided, and the attendance was excellent. Officers for 1957-58 are: President, Dr. R. O. Jones of Halifax; Vice-President, Dr. A. MacVicar of Charlottetown; Secretary-Treasurer, Dr. M. Mendelson of Halifax.

The training seminar of the N.B. Division, Canadian Cancer Society, held in Sackville was successful and during its sessions the local branch presented a cheque for $14,828 to the National Cancer Institute to support research. Distinguished guest speakers included Dr. R. M. Taylor, Executive Director of the National Institute, and Professor Ian Campbell of the Department of Sociology at Mount Allison University.

A. S. KIRKLAND

NOVA SCOTIA

Dr. N. H. Gosse and his wife, Dr. Margaret Gosse, recently visited Istanbul as part of the Canadian delegation to the General Assembly of the World Medical Association. Dr. N. H. Gosse delivered a paper on the utilization of hospitals and medical care in Canada and the United States. He also availed himself of the opportunity to visit medical centres in the Mediterranean area. Dr. Gosse attended the 1955 assembly in Stockholm, at which time he also visited medical centres concerned with the diagnosis and treatment of cancer.

WALTER K. HOUSE

FUTURE C.M.A. MEETINGS

1958 Halifax	June 16 - 20
1959 Edinburgh (Conjoint meeting with B.M.A.)	July 16 - 24
1960 Banff	June 13 - 18

BOOK REVIEWS

GUIDE TO MEDICAL WRITING. Henry A. Davidson, Editor of the Journal of the Medical Society of New Jersey. 338 pp. Illust. The Ronald Press Company, New York, 1957.

Scripta manent, the Ancients used to say. Paraphrasing them in his preface, the author writes, "once you have launched the article into print, it becomes immortal. It remains forever in the archives of your profession. If it is a poor job, its ghost will haunt you, for not one bad word of it can ever be erased." Thus justifying the importance of his subject and denying that he is a mere "sadistic wielder of the blue pencil", he proceeds to give the prospective author one of the most useful and readable concise treatises on the art of medical writing. Starting with the choice of the topic, he points out that "what makes a paper valuable is not necessarily an absolute novelty of content. An article is valuable if old material is refiltered through the author's own experience." Although the reporting of laboratory results and experimental data may be hard enough to master, clinical papers devoted for instance to the evaluation of a new drug present even greater difficulties. Useful advice is given on the collection of data and the scanning of background literature. The actual writing of the article covers five chapters. Except for an undue insistence on eye catchers and dramatic presentation, all the recommendations contained therein are eminently practical. A brief section is devoted to medical statistics which are presented in an elementary manner, with simple words and incisive remarks. Notes on reporting case histories and w iting abstracts, book reviews and meeting reports are also presented. The section devoted to pictures and graphs may concern more directly photographers and medical artists, but still is of general interest to the medical author. Dr. Davidson has been connected with medical reporting for over 25 years, and his experience as an editor will be of use to the tyro and the prolific contributor alike. As nearly every physician at one stage or another of his career is called upon to put his thoughts into print, the book is highly recommended to the profession at large.

MENSCHLICHE UND TIERISCHE GEWEBSTHROMBOKINASEN (Human and Animal Tissue Thrombokinases). H. A. Thies, Hamburg, W. Germany. 56 pp. Illust. Georg Thieme Company, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1957. $2.85.

When Dr. Thies began to study anticoagulant therapy in Hamburg in 1948, he found little guidance from publications elsewhere. Difficulties in particular arose in relation to determination of thromboplastin. This led to an extended study of thrombokinases. Extracts from grey, white and mixed human brain substance, human muscle, lung, liver, spleen and testis as well as preparations from domestic animals and industrial thrombokinases were studied. This monograph describes the work done on the preparation and the evaluation of thrombokinases; their significance in anticoagulant therapy is also discussed.

COLD INJURY. Transactions of the Fourth Conference, November 7, 8 and 9, 1955. Edited by M. Irené Ferrer, Department of Medicine, Columbia University, New York. 371 pp. Illust. The Josiah Macy, Jr. Foundation, New York, 1956. $5.95.

The Fourth Conference on Cold covers a wide range of topics with the interesting addition of studies relating to supercooled and frozen mammals and physiological studies in general hypothermia leading up to its application to cardiac and brain surgery.

The subject of local cold injury, or frostbite, and related states is as usual discussed in an informal and complete manner by authorities in the field. Soft tissue and bone reactions in the experimental animal and in man are noted. None of the experimenters has found an animal's extremity that is similar to a human foot, and conclusions drawn from observations of a rabbit's hind leg must be carefully considered before any resulting principles of treatment are applied to humans.

There are a multitude of stimulating thoughts expressed in this free discussion, and students of local or general hypothermia would be well advised to read this monograph.

MEDICAL NEWS *in brief*

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POLIOMYELITIS IN U.S.A.

In a recent statement, Surgeon General Leroy E. Burney of the U.S. Public Health Service reported that there have been 1576 cases of paralytic poliomyelitis so far this year in the U.S.A., compared with 7886 for the same period in 1955 and 5241 in 1956. Only 63 cases of paralytic polio have been reported among the 28 million persons who have received three injections of vaccine, and not all of these cases have yet been confirmed. Although the vaccine is designed to prevent paralytic poliomyelitis as distinguished from the non-paralytic form, the total number of polio cases this year also shows a sharp reduction. There have been 4851 cases so far, compared with 21,667 two years ago, 12,146 one year ago and an average of 24,928 a year over the past five years.

RESPIRATORY ALTERATIONS ASSOCIATED WITH OBESITY

The association of somnolence and cyanosis with extreme obesity has recently been recognized as part of a syndrome which also includes periodic breathing of the Cheyne-Stokes variety, polycythæmia, right axis electrical deviation on the electrocardiogram and clinical appearance of congestive heart failure. Members of the Department of Medicine, Duke University School of Medicine, and Veterans Administration Hospital, Durham, North Carolina, report on a series of six such cases (*Circulation*, 16: 179, 1957). The syndrome is also known as alveolar hypoventilation and is supposedly the result of a decrease in total lung volume and in functional residual capacity, particularly marked in the supine position, leading to reduced arterial oxygen saturation. The degree of obesity at which the syndrome becomes manifest is not well defined. The authors point out that most of their patients had gained large amounts of weight in the six to 12 months preceding the onset of symptoms. Thorough laboratory investigation failed to

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MEDICAL NEWS *in brief*

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reveal any particular endocrine disturbance. These cases were characterized by high oxygen consumption and low blood cholesterol level. It is significant that the symptoms subsided with loss of weight, even when the patients were still far beyond the limits of their ideal weight-to-height ratio. The periodic breathing is considered to be of central origin although its exact mechanism still remains obscure.

MEDICAL FILM OF THE MONTH

The Medical Film Guild Limited, 506 West 57th Street, New York 19, N.Y., reports that the "Medical Film of the Month" subscription series introduced a year ago for postgraduate and undergraduate medical training has proved so popular among medical societies, hospitals, clinics and schools of the United States and Canada that many vital new subjects are being added for the program of the coming year. These films can also be used in nursing schools and medical conventions, and some of them have been designed for lay audiences. A list of the films available and their rental charges can be obtained by writing to the above address.

BOOKLET ON VARICOSE VEINS

The American Heart Association has just published a short booklet on varicose veins, directed to the lay public. It contains brief descriptions in simple words of the cause of this vascular defect together with the various means of arresting or correcting it. There is nothing new in it that a conscientious doctor has not already told his patient, but it could help the patient who may not remember all the details which he was given within a matter of a few minutes in the doctor's office. Copies may be obtained by writing the American Heart Association, 44 East 23rd Street, New York 10, N.Y.

HANDBOOK FOR OSTEOARTHRITICS

Most practising physicians have osteoarthritic patients to look after, and would welcome assistance in helping their patients to live with a minimum disability. The Canadian Arthritis and Rheumatism Society has recently published a booklet "Osteoarthritis – A Handbook for Patients" which should be really beneficial to any physician wanting to educate his osteoarthritic patients. The booklet is not given to patients and is not designed for self-treatment. The only way in which the patient can obtain this booklet is from his doctor, and physicians are therefore requested to write for these booklets to the Canadian Arthritis and Rheumatism Society, National Office, 900 Yonge Street, Toronto 5, Ontario, or to their provincial division. The price is just 25 cents, and the book is certainly worth a lot more. It tells the patient in simple language what osteoarthritis is and what it is not; it summarizes the management of the disease and gives advice on proper posture, heat treatments suitable for use in the home, and therapeutic exercises for osteoarthritis.

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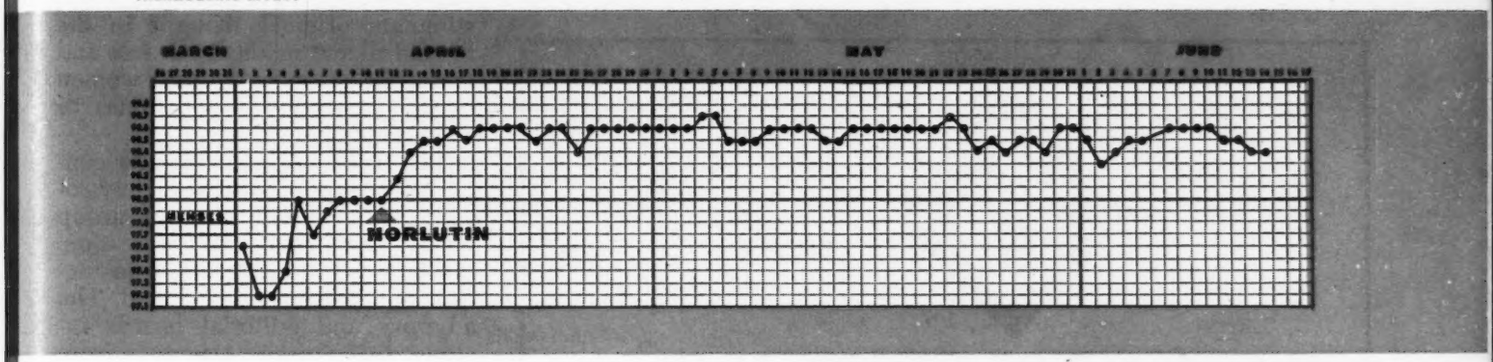

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*Greenblatt, R. B.: *J. Clin. Endocrinol.* 16:869, 1956.

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MEDICAL NEWS *in brief*

(Continued from page 54)

CANADIAN TUBERCULOSIS ASSOCIATION ANNUAL MEETING

The 58th annual meeting of the Canadian Tuberculosis Association will be held in Quebec City at the Château Frontenac on June 9 to 12, 1958. General sessions which will be of interest to both professional and lay groups have been planned for two days. There will also be two days of sectional meetings for physicians, nurses, rehabilitation officers and provincial tuberculosis associations.

Detailed information may be obtained by writing to the Canadian Tuberculosis Association, 265 Elgin Street, Ottawa 4, Ont.

PERSPECTIVES IN BIOLOGY AND MEDICINE

The Division of Biological Sciences and the Press of the University of Chicago announce the appearance of a new quarterly journal with a multidisciplinary approach to the problems of biology and medicine and entitled *"Perspectives in Biology and Medicine"*. The editors are Dr. Dwight J. Ingle and Dr. S. O. Waife and the intention is stated to be the production of a journal oriented towards man and his diseases, with appreciation of the fact that roots of medical theory reach to all fields of biology and all processes of life. It is intended to communicate and stimulate original thought in the biological and medical sciences and to inspire young men and women to think beyond the confines of specialization.

The first issue will include contributions on a wide variety of subjects including creative group therapy, stress, medical education, biochemical genetics, insulin action, and the legacy of Freud. The advisory and editorial boards include distinguished scientists from the United States and other countries; Canadian representatives include M. J. Berrill and Theodore Rasmussen of McGill University. Subscriptions at $6.00 a year may be sent to the University of Chicago Press, 5750 Ellis Avenue, Chicago 37, Illinois, U.S.A.

LOW VISION CLINIC

A special clinic for low vision patients, jointly sponsored by the University of Toronto and the Canadian National Institute for the Blind, has been established under the direction of Dr. D'Arcy Macdonald of the Department of Ophthalmology, University of Toronto and the Toronto Western Hospital.

This clinic is held in the outpatient eye clinic at the Toronto Western Hospital and patients may be seen by referral from the C.N.I.B. or from ophthalmologists.

LEDERLE RESEARCH FELLOWSHIPS

The awarding of eleven Lederle of Canada Research Fellowships for study at universities in Nova Scotia, Ontario, Quebec and Saskatchewan has been announced by Joel R. Brown, Jr., manager of Lederle Laboratories Division, North American Cyanamid Limited.

(Continued on page 58)

1. Miller, J. M.; Surmonte, —. A.; Ginsberg, M., and Ablondi, F. B.: Streptokinase Intramuscularly in the Treatment of Infection and Edema. (Scientific Exhibit) *Postgraduate Medicine* Vol. 20, No. 3: 260-267 (Sept.) 1956.

Postgraduate Medicine

"OBSERVATIONS ON THE INTRAMUSCULAR USE OF STREPTOKINASE[1]

1. Most patients showed beneficial clinical effect after 24 hours.
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11. No chills, cyanosis or allergic reaction.

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PRECAUTIONS

1. An antibacterial drug must be given with the intramuscularly administered streptokinase.
2. Streptokinase should not be given to patients known to have defects in the clotting mechanism."

†No fibrinolysis detectable in circulating blood stream.

MEDICAL NEWS *in brief*

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Names of the fellowship winners and their fields of research follows:

Dalhousie University: Gerald Berry, Montreal, pathology; W. P. Warren, Halifax, pharmacology.

University of Ottawa: Marc Colonnier, Ottawa, anatomy; Anita Jakerow, Ottawa, pharmacology.

University of Toronto: Donald R. Hopkins, York Mills, Ont., physiology; Harry Schachter, Toronto, physiology.

University of Western Ontario: Norman A. Fretz, London, physiology; Kathleen M. Sandor, London, biochemistry.

University of Montreal: Christian Lamoureux, Montreal, biochemistry; Yves Langlois, Cartierville, physiology.

University of Saskatchewan: Suzanne Yip, Saskatoon, biochemistry.

III WORLD CONGRESS OF CARDIOLOGY

The III World Congress of Cardiology will be held in Brussels, Belgium, from September 14 to 21, 1958. Anyone wishing to present a scientific paper at this congress should submit an abstract in French or English, not exceeding 200 words, by February 1, 1958, to: Dr. Robert S. Fraser, Secretary-Treasurer, Canadian Heart Association, University of Alberta Hospital, Edmonton, Alberta.

MOTION PICTURE FOR CARDIAC PATIENTS

Rehabilitation sections of cardiovascular units throughout the country will be interested in a new motion picture called "Take Three Hearts", which has been released by the American Heart Association and its affiliates. It tells the stories of a housewife, a carpenter and a school child suffering from different forms of heart disease and dramatizes the ways in which local Heart Associations help restore them to useful and happy living. This 16-mm., 27-minute sound film in black and white is available from local Heart Associations or from the American Heart Association, 44 East 23rd Street, New York 10, N.Y.

THE WILLIAM OSLER MEDAL

In order to stimulate interest and research in medical history among students of the medical schools of the United States and Canada, the American Association of the History of Medicine has established a medal that will be granted annually to the author of the best essay submitted to the Association. The medal has been named in honour of William Osler, who more than any other academic teacher succeeded in creating among students enthusiasm for the history of medicine.

The Association will consider unpublished essays by men and women who were students in schools of medicine and had not obtained their doctor's degree at the time the essay was written. To be considered, an essay must be submitted before or within one year after the author's graduation.

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(1) Martel, A.: Preludin (Phenmetrazine) in the Treatment of Obesity, Canad. M.A.J. 76:2, 1957. (2) Pattee, C. J.: Phenmetrazine—A New Anti-Appetite Drug, Can. Serv. Med. J. 13:3, 1957. (3) Robillard, R.: Preliminary Study of Preludin during Treatment of Obesity in Diabetes Mellitus, Canad. M.A.J. 76:11, 1957. (4) Joncas, F., and Bissonnette, J.: Obésité et Diabète—Evaluation clinique d'un nouvel agent anorexique, Préludine (phenmétrazine), Union méd. Canada 86:6, 1957. (5) Natenshon, A. L.: Am. Pract. & Digest Treat. 7:1456, 1956. (6) Gelvin, E. P.: McGavack, T. H., and Kenigsberg, S.: Am. J. Digest. Dis. 1:155, 1956.

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MEDICAL NEWS *in brief*

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Essays that are the result of original research will be given preference, but the Association will also consider essays which, without being the result of original research, show an unusual appreciation and understanding of historical problems.

Essays should not exceed 10,000 words in length. They must be sent before April 1, 1958, to: Dorothy M. Schullian, Ph.D., Chairman, National Library of Medicine, History of Medicine Division, 11,000 Euclid Avenue, Cleveland 6, Ohio.

INTRAVENOUS PRESSURE

Dr. H. O. Sieker of the Veterans Administration Hospital, Durham, North Carolina, has recently been using a device developed by Dr. O. H. Gauer, for reading blood pressure in the veins and the heart chambers. The meter is the size of a match-head and contains a small float that hangs freely in a magnetic field. Slight variations in blood pressure make the plunger move and cause electric impulses which are transmitted along flexible plastic wires to be amplified and recorded. The technique, which is similar to that of catheterization, has been used in about 25 subjects in each of whom 50 to 100 different readings have been taken.

POSTGRADUATE COURSES

The annual, short postgraduate courses in Internal Medicine, Neurology, Obstetrics and Gynæcology, Ophthalmology, Otolaryngology, Pædiatrics, and Radiology will be given during March and April 1958 at the University Hospital, Ann Arbor, Michigan.

INTERNATIONAL SOCIETY OF HÆMATOLOGY

The Seventh Congress of the International Society of Hæmatology will be held in Rome, Italy, at the Palazzo dei Congressi, EUR, from September 7 to 13, 1958. Prospective contributors having research data in this field which they consider worthy of presentation should write to the Secretary, Professor Cataldo Cassano, at the Istituto di Patologia Medica, Policlinico Umberto 1, Roma, Italy. Information concerning attendance and participation in this meeting may be also obtained from Dr. Sol Haberman, Secretary General Western Hemisphere, Baylor University, 3500 Gaston Avenue, Dallas, Texas.

INTERNATIONAL FEDERATION OF GYNÆCOLOGY AND OBSTETRICS

The Second World Congress of the International Federation of Gynæcology and Obstetrics will take place in Montreal, June 22-28, 1958. Every gynæcologist and obstetrician in Canada is invited to attend this meeting, which will be under the distinguished patronage of His Excellency the Right Honourable Vincent Massey, C.H., Governor General of Canada. The theme of the meeting will be "Current Trends in Gynæcology and Obstetrics". Participants have until December 31, 1957, to file their application. A preliminary program will be sent to those who will have registered before March 31, 1958. Meetings will be held in the Queen Elizabeth Hotel, Dorchester Street West, Montreal. All

those interested should communicate with the Montreal Committee, Second World Congress, The International Federation of Gynæcology and Obstetrics, Suite 220, 1414 Drummond Street, Montreal 25, Canada.

INFLUENZA IN CANADA

In November, 27.7% of the 17,000 school children of Halifax were absent. Larger firms in the district reported absenteeism in 10-15% of their clerks. In Quebec the epidemiologist reported that in the eastern part of the province the epidemic was still increasing, involving about 10% of the population, with schools closing; in the central region the epidemic was at its peak, the schools were closed and about 25% of the population were sick; in the western part the schools were reopening, the epidemic was decreasing and only about 5% of the population were still affected. The Chief Medical Officer of Health of Ontario reported a general decrease in the incidence of influenza throughout the province. Absenteeism in the schools and in industry was practically back to the level expected at this time of year. In Manitoba, it was estimated that 30 to 40% of the population of Deloraine and district was suffering from the disease. In Alberta the percentage of the population affected by the current epidemic ranged between 15 and 40%; however, an outbreak involving approximately 90% of the population of the Cold Lake Indian Reserve had been reported by local health authorities. Admissions to the Vancouver General Hospital (B.C.) for serious respiratory infections were slightly above normal for this time of year.

In the rest of the world the reopening of the schools after the summer holidays appears to have influenced a certain recurrence of influenza in Asia, Japan and Turkey, for example. The coming of winter appears to affect the length and extent of the epidemic in other parts of the northern hemisphere; it seems, however, that its maximum has already been reached or passed in several regions of the United States and Central Europe. The mortality attributed to influenza and to pneumonia, as well as the general death rate, has increased for the past few weeks in those countries where the disease is widespread; up to the present, however, there has been no definite sign of an increase in the virulence of the disease.

BED REST IN PULMONARY TUBERCULOSIS

A report of the Sub-committee on Bed Rest in Pulmonary Tuberculosis, American College of Chest Physicians, points out that there has been some relaxation in the strictness of application of bed rest in treatment of pulmonary tuberculosis since the advent of chemotherapy. However, it is generally considered as a basic requirement of therapy in spite of deliberate programs in some areas to minimize the importance of bed rest for the purpose of investigation. Those in active practice in chest diseases generally understand and accept the need for bed rest, but the person who casually reviews the literature may gain an erroneous impression in this respect. Since an increasing amount of

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tuberculosis is being cared for by those not specially trained in this disease, lack of information on the whole treatment picture may lead to disastrous results. It is the feeling of the committee that the importance of bed rest and its proved value in tuberculosis treatment should be reaffirmed, and that this statement should receive the widest possible attention. It is believed that bed rest should be maintained until the lesion is stabilized, as indicated by bacteriological, x-ray and clinical evidence. The committee also reaffirms the desirability of at least starting the patient's care under sanatorium conditions for patient indoctrination, evaluation of his clinical problem, and initiation of the various therapies.

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FALSE CLAIMS FOR ASIAN INFLUENZA MEDICINES

The Federal Trade Commission and the Food and Drug Administration of the United States will take prompt action if manufacturers make false or misleading claims that their drug products are effective in preventing or treating Asian influenza. The Food and Drug Administration has warned the public to be on guard against unwarranted claims for Asian influenza medicines and has advised them to consult a physician for proper and safe means of prevention and treatment of the disease. Vigorous enforcement action will be undertaken by the FDA if necessary under the Federal Food, Drug and Cosmetic Act.

The Federal Trade Commission which enforces the Federal law against false advertising said that it would check all advertising media and would move promptly to eliminate any claims that were false or misleading.

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BANTING RESEARCH FOUNDATION GRANTS

The Banting Research Foundation announces eight new grants ranging in value from $600 to $2000 to finance medical research. Grants have been made to the following research workers:

Dr. A. C. Abbott, Abbott Clinic, Winnipeg, for research on the experimental plastic repair of ureter with an isolated loop of ileum; Dr. W. St. Clair Bauld, Department of Metabolism, Montreal General Hospital, for investigation of conjugated œstrogens in human pregnancy urine; Dr. S. H. Bensley, Department of Anatomy, University of Toronto, for study of mast cells and connective tissue lesions; Dr. K. A. C. Elliott, Montreal Neurological Institute, for studies on gamma-aminobutyric acid and other inhibitory substances in brain; Dr. R. E. Haist, Department of Physiology, University of Toronto, for studies on adrenal function; Dr. Werner Kalow, Department of Pharmacology, University of Toronto, for electrophoretic studies on aromatic esterase of

human serum; Dr. David A. Rosen, Department of Ophthalmology, Queen's University, for study of the effect of the Valsalva experiment on intraocular pressure of normal and glaucomatous eyes; Mr. H. Singh, Department of Pharmacology, University of British Columbia, for studies of activation of smooth muscle.

Requests from six other investigators for sums totalling $10,000 could not be granted owing to the limited funds available.

THE SMALLPOX HAZARD

No fewer than 18 countries were infected with smallpox by international travellers in 1956, and as a result eight of them suffered epidemics of this quarantinable disease, according to the WHO Committee on International Quarantine.

At a recent meeting in Geneva, the Committee warned against any relaxation of vaccination measures against smallpox and called for the use of potent vaccines as well as correct vaccination procedures. Moreover, the Committee stressed the need for medical and other personnel who come in contact with travellers to maintain a high level of immunity against smallpox by repeated vaccination. In the course of these epidemics, some doctors treating tourists caught the infection and died. The WHO experts also drew attention to the advantages of dried smallpox vaccine for mass campaigns. Dried vaccine is easily transportable, remains effective without refrigeration and does not spoil, even in the tropics.

The eight countries where smallpox epidemics took place were: Ceylon, Ghana, Iran, Italy, Lebanon, Sierra Leone, Sudan, and the United Kingdom.

FIRST AID AND TRANSPORTATION OF THE INJURED

A new activity of the Saskatchewan Division Committee on the Medical Aspects of Traffic Accidents is reported from Regina. Dr. W. H. E. Alport of the Saskatchewan Division, C.M.A., organized a meeting on first aid and transportation of the injured in that city on October 17. Two half-hour lectures were given on "Do's and Dont's" at the scene of a serious accident, one from the viewpoint of a neurosurgeon and one from the viewpoint of the orthopædic surgeon. The meeting was then thrown open for questions and discussion. Discussion was extremely lively and spirited, and those attending felt that the meeting had been very worthwhile. R.C.M.P. Traffic Officers were particularly interested and suggested a repetition of these sessions. Ambulance drivers from Regina and Moose Jaw were present, together with city and R.C.M.P. Traffic Officers, Highway Traffic Board Officers and others. The speakers were Dr. Bachynski and Dr. Ryan.

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The success of this meeting has induced the Committee to plan a similar session in Saskatoon this winter and to invite traffic personnel from the northern half of the province. It is also hoped to continue this as an annual program.

FELLOWSHIPS IN RADIOBIOLOGY

The Defence Research Board invites applications for a fellowship in radiobiology tenable in certain designated universities, or other scientific centres, in the United Kingdom. Candidates must be Canadian residents who are graduates of an approved university; they may have a medical degree or one in biology and biophysics. Awards are for persons to work in basic medical sciences, and with an interest in laboratory research. The fellowship will be tenable for one year with renewal if progress is satisfactory. The value of the award is $3000-$5000 per annum. After training, the candidate will be expected to establish himself in a suitable university or other research centre in Canada. Applications for the fellowship should be submitted on the approved form together with supporting documents to Chairman, Defence Research Board. Forms are obtainable from Grants Office, Defence Research Board, Department of National Defence, Ottawa. Closing date for applications is February 1, 1958.

MARKLE FOUNDATION GRANTS

In the annual report of the John and Mary R. Markle Foundation, appropriations of $1,409,000 during 1956-57 were announced. The largest appropriation, $750,000, was given to support 25 selected teachers and investigators in U.S. and Canadian medical schools to continue the Foundation's Scholar in Medical Science program. This includes two Canadian scholars, Drs. Aurèle Beaulnes of the University of Montreal and Robert O. Morgen of McGill.

Two grants totalling $212,000 were made to Duke University School of Medicine and the University of Cincinnati College of Medicine to strengthen the position of the preclinical sciences. In addition McGill University Faculty of Medicine received a grant of $30,000 to move the Osler Library to the Medical Sciences Centre and of $22,500 for cataloguing the Library and related historical material.

PRIZE FOR MEDICO-SURGICAL FILM

The Annual Prize for Medico-Surgical Films, awarded by *La Presse Médicale* and amounting to 100,000 Fr. francs, will be given during the final session of the course on "Actualités Médico-Chirurgicales" at the Faculté de Médecine de Paris in March 1958. The teaching value of the film as well as its cinematographic quality will be considered. Only 16-mm. films can be entered. Applications and films should be sent to: Secrétariat du Journal *La Presse Médicale,* 120 Boulevard Saint-Germain, Paris VI°, France, before February 15, 1958.

This year, for the first time, films subsidized or produced by a laboratory or company will be eligible for awards.